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The American Heart Journal

VOL. II APRIL, 1927 No. 4

Original Communications

ON THE COMBINATION OF ANGINA PECTORIS AND SEVERE ANEMIA*

JAMES B. HERRICK, M.D.
CHICAGO, ILL.

IN 1918 Herrick and Nuzum,[1] in an article on angina pectoris, called attention to the occasional association of angina pectoris and severe anemia. I quote: "We have been interested in four patients with high grade anemia who described perfectly typical anginal attacks on walking—constriction, pain, radiation, erect posture, immobility. One man in the terminal stages of pernicious anemia died in an anginal seizure. Another with a marked anemia of secondary type with neoplasm in the abdomen improved under digitalis so far as the cardiac manifestations were concerned. A third died of his metastatic carcinomas appearing after the amputation of the penis for the primary tumor. A fourth was lost sight of; his severe anemia was of doubtful origin, suspiciously like pernicious anemia. To what extent the anemia was a contributing or causative factor in these four cases can only be conjectured; or perhaps the association was purely accidental. In none was there a necropsy. One may surmise that blood of poor quality going through somewhat narrowed coronaries might favor the development, on slight provocation, of an anginal spell, that is, if one accepts the coronary—intermittent claudication—origin of the pain. We have thought of the possibility of a tumor's being so located as to cause coronary obstruction or so as to involve the wall of the beginning aorta. But in two of these cases there was no reason to suspect tumor anywhere in the body. Necropsies in cases of this type might be illuminating."

So far as I know this is the first direct reference to this combination of diseases or this association of symptoms. Since 1918 I have seen three other similar cases. One was in an adult male with a typical pernicious anemia and an angina of effort. A second concerned

*Read before The Society of Internal Medicine of Chicago, February 28, 1927.

a nonluetic man of seventy, with evidence of vascular and myocardial degeneration as shown by dyspnea, often nocturnal, numerous extrasystoles and characteristic substernal pains on walking. After more than a year of annoying cardiovascular disturbance a severe anemia became manifest. This had the characteristics of pernicious anemia and was the immediate cause of death. The anginal manifestations lessened as he was confined to the house and finally became bedridden.

The third case was that of a man, sixty-three years of age, who came to me in the Presbyterian Hospital, January 4, 1924, complaining of marked hematuria of more than one year's duration, pain in the right lumbar region, pallor, emaciation, dyspnea and weakness. Also, for one year there had been pain in the chest on walking. At first this pain appeared only on walking a long distance. Gradually the amount of effort necessary to bring on the pain lessened until walking thirty feet, or even moving about the room, would bring it on. At first he gave up walking to his office; for a time he used the street car, then a cab and finally had to remain at home. The pain often began in the left arm, then passed to the chest. It was severe in the sternal region, made him stand still. He felt sure that death would have followed a continuance of walking. In the past history there was nothing of moment except that since 1920 he had occasionally had attacks of vertigo of the Ménière type, some of them quite severe. There was no history of syphilis.

As a result of an extended study of the case, including pyelography and microscopical examination of a gland cut out from the neck, a diagnosis was made of carcinoma of the right kidney with metastases, gall stones, Ménière's disease, severe secondary anemia, arteriosclerosis, and angina pectoris

The features of the case that have to do with the present discussion are the anemia and the cardiovascular findings. On admission he was extremely pale with a high grade secondary anemia, the red cells being 2,240,000, hemoglobin 16 per cent, white cells 6850. The anemia seemed accounted for by the cachexia due to the neoplasm and by the loss of blood, which at times had been in such large amounts as to alarm not only the patient but his doctor. Cystoscopic examination showed that the bleeding was from the right kidney. Under prolonged rest in bed the patient had less lumbar pain and less blood in the urine, though there was always some. The hemoglobin rose so that by March 1, 1924, it was 32 per cent and the red corpuscles increased to 3,900,000.

The heart was not greatly enlarged. The peripheral arteries, as the temporal and radial, were tortuous and firm-walled. While the patient was in the hospital no attacks of angina occurred.

He died May 17, 1924, from general exhaustion due to the malignant growth. Autopsy showed carcinoma of the right kidney, metas-

tases in liver, lung, glands, etc., gallstones, marked senile arteriosclerosis of the aorta and coronary arteries. The left coronary was sclerosed and solid from its mouth to its division into the left anterior and descending branches. Both these branches had calcified plaques. The muscle of the heart showed fatty infiltration with areas of fibrosis.

The association of angina pectoris with severe anemia is not common. At least this is true in my own experience, for though in the last nine years I have been on the watch for these cases, I have seen only three. During this period I have seen quite a number of cases of severe anemia and what one may call a large number of cases of angina pectoris, a number running into the hundreds. The experience of others seems to bear out the statement as to its relative infrequency, though I cannot substantiate it by presenting the results of an exhaustive search of the enormous literature of pernicious anemia and angina pectoris. I have, however, kept an eye on current medical literature and have been at pains to consult certain statistical papers for the express purpose of seeing if there were recorded cases of this character. They are very infrequent.*

There is an occasional case that might be cited but the authors lay no stress on the association, mentioning it only in a casual way.

For example, Sturgis[11] while writing of angina pectoris as a complication of myxedema and exophthalmic goiter describes the case of a woman with myxedema and anginal attacks whose blood showed at one time 2,000,000 red corpuscles and 45 per cent of hemoglobin. An atheromatous aorta with tortuous, firm coronaries and fibrous patches in the myocardium were found at autopsy after her sudden death. No special connection between the anemia and angina is suggested. He also observed angina in a man of fifty-seven years with myxedema who had a moderate grade of secondary anemia, the hemoglobin being 53 per cent. Under thyroid treatment there was improvement in the myxedema and angina. Whether the blood condition was also bettered is not stated.

W. Hunter[12] cites a case of pernicious anemia in a physician who, in what Hunter calls a severe toxemic attack, had frequent prolonged attacks of heart pain. In another the patient himself refers to the frequent severe attacks of angina. The patient recovered and there was no anginal residue two years later though there were some sensory disturbances as in the cord symptoms of pernicious anemia.

In the last two years, however, the subject has attracted the attention of at least two writers. In Argentina Bullrich[13] describes the condition, and cites seven cases in his own practice. Bullrich's ob-

*Levine and Ladd[2] in 150 cases of pernicious anemia; Willson and Evans[3], 111 cases; Campbell and Conybeare[4], 75 cases; Giffin and Bowler[5], 628 cases; Braun[6], 127 cases; Rohner[7], 127 cases; Carr[8], 148 cases; Panton and others[9], 117 cases, make no mention of anginal pain. Reid[10] discussing the heart in pernicious anemia makes no mention of angina.

servations are independent ones, he had not seen the paper of Herrick and Nuzum several years before nor any other pertinent references to the subject. In the discussion of his paper in the meeting of the Argentine Medical Society in Buenos Aires Ivanissevich reported a case of his own.

In England Carey Coombs[14] describes eight cases citing the Herrick and Nuzum paper as the only reference to this subject that he has seen. The paper of Coombs drew forth a brief report of a case by Evans.[15]

From personal conversation with a few Chicago physicians I find that some have not seen the combination, others have. Dr. Giffin of the Mayo Clinic in November of last year discussed it in a clinical meeting at Rochester, Minnesota.

While relatively rare, therefore, it is of occurrence frequent enough to deserve mention and to arouse interest as to its origin and significance. It may also happen that when attention is more pointedly drawn to the subject many more cases will come to light and the condition will be found to be more common than it is now thought to be.

In our paper of 1918 we suggested that with blood of poor quality going through narrowed coronary arteries angina might be produced more easily than with normal blood going through the same arteries. This, it will be noticed, assumes that the coronaries are directly concerned in the production of anginal pain. It really invokes the theory of relative ischemia of the myocardium due to defective coronary blood supply to explain the pain. One might say in these cases that due to the anemia the threshold of pain is lowered so that pain is manifested on slighter provocation. Coombs expresses the thought thus: "The incidence of cardiac pain in cardiosclerosis with pernicious anemia is higher than in cardiosclerosis alone."

Bullrich advances and elaborates this view. He believes that, as was true in his patients, there is a substratum of cardiovascular, i.e., coronary change. When to this circumstance, which leads to a poor blood supply to the myocardium, there is added a deficiency of nourishment through deterioration of this blood, diminishing still further the functional capacity of the myocardium, angina may easily occur. The lessening of the angina in some of his patients as the condition of the blood improved is advanced by him as an argument—it seems to me a valid one—for the view that the anemia is a contributing factor. Coombs also refers to patients whose angina lessened as the anemia disappeared. In my last case the disappearance of the cardiac pain was coincident with the bettering of the blood state, though the influence of quiet cannot be eliminated as an explanation. One may question also whether in some of Bullrich's cases the antisyphilitic treatment may not have altered the vascular as well as blood condition and in this way helped to lessen the angina.

All that one may justifiably conclude is that there is occasionally seen a combination of angina pectoris with severe anemia, which anemia is often, though not always, of the pernicious type. This combination may at times be purely accidental. At other times though there is usually a ground-work for angina in cardiovascular lesions, the anemia is a factor contributing to the production of the painful seizures.

There is perhaps a lesson to be drawn from all this. In some of our patients with angina pectoris might not therapy directed toward the improvement of the blood work beneficially in relieving the pain? Iron and antisyphilitic remedies, climatic and other hygienic measures, the removal of foci of infection, diets suited to increase the nutrient properties of the blood,—perhaps such as those recommended in cardiac cases, diets rich in sugar and other carbohydrates—might be helpful.

Also as a corollary, one feels inclined to advance this combination of conditions as an argument for the coronary artery and myocardial ischemia theory of angina as opposed to the aortic theory.

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THE DISTURBANCES OF THE CARDIAC MECHANISM IN SUBACUTE BACTERIAL ENDOCARDITIS AND RHEUMATIC FEVER*

M. A. Rothschild, M.D., B. Sacks, M.D., and E. Libman, M.D.
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SOME years ago one of us made the observation that patients suffering from chronic valvular disease with auricular fibrillation rarely develop subacute bacterial endocarditis, and conversely, that it is unusual for patients with subacute bacterial endocarditis to develop fibrillation.[1] These observations led to an investigation of the disturbances of the cardiac mechanism in a series of cases of this disease. We were struck not only by the infrequency of gross irregularities in the heart rhythm, but also by the rarity of changes in the ventricular portion of the electrocardiogram, although we had noted such changes in a high percentage of cases of rheumatic fever. Our findings were briefly presented in 1923,† and in this communication we wish to make a more complete report.

CARDIAC MECHANISM IN SUBACUTE BACTERIAL ENDOCARDITIS

One hundred and twenty-three cases of subacute bacterial endocarditis were investigated. The suspected etiology of the pre-existing cardiovascular impairment was ascertained in sixty-six cases. Of these, thirty-four gave a history of rheumatic fever (including chorea), thirteen of repeated attacks of tonsillitis or sore throat, nine of syphilis, and eight of scarlet fever In the remaining five, the subacute streptococcus infection was superimposed upon a patent ductus arteriosus. Valvular disease was present in 118 cases, the incidence of mitral stenosis being 46.6 per cent. The average duration of the cardiac defect upon which the bacterial infection was presumably engrafted was ten years in forty-one patients from whom satisfactory data could be obtained. Because of the insidious onset of the symptoms, the figures for the duration of the bacterial endocarditis itself are probably not altogether reliable. In most cases the onset of the bacterial infection probably antedated the patient's earliest symptoms. A more or less definite account of the actual time of onset was obtained in seventy-nine cases, and in these the average duration was about six months. Twenty-seven patients were under observation for periods varying from six months to two years.

*From the Medical Department and the Laboratories of the Mount Sinai Hospital.
†Before the American Society for Clinical Investigation, Atlantic City, May, 1923.

In describing the findings, a distinction will be made between the active and bacteria-free cases. In the former, there are the usual signs and symptoms of the disease, most of the patients dying with bacteria still in the circulation. Some of the patients, however, lose their bacteremia while under observation, but subsequently succumb to the sequelae of the disease. At autopsy, the characteristic endocardial lesions are found, but they have undergone healing with fibrosis, hyalinization and calcification, and no longer contain bacteria in spreads and sections. This constitutes the bacteria-free or healed stage, and in many cases the patient does not enter under observation until already in this stage. Negative blood cultures alone do not establish the diagnosis of the bacteria-free stage, for in a certain number of active cases in which blood cultures are persistently negative, myriads of bacteria are discovered in the endocardial vegetations at autopsy, not only in cultures but also in sections. Such cases are merely instances of active subacute bacterial endocarditis in which the circulating bacteria could not be cultivated. The bacteria-free stage on the other hand is characterized by the healing (in a pathological sense) of the endocardial lesions and by the absence of bacteria in sections. The patient is not cured, however, but generally succumbs to the mischief done to the heart valves, myocardium, hematopoietic system, or kidneys during the active or bacterial stage of the disease, or to embolism or intercurrent infection.[2, 3, 4, 5] Of the 123 patients studied, 109 were in the active or bacterial stage.

Blood cultures were taken in 104 of the active cases, and bacteria cultivated in 84, or 80.8 per cent.* The anhemolytic streptococcus (Streptococcus viridans) was isolated in 79 cases, the gonococcus in three, and the influenza bacillus in two. The diagnosis in the fourteen bacteria-free cases was verified by autopsy in all but two. Of the entire group of 123 cases, all except a few are known to be dead.

Graphic evidence of the cardiac rhythm was obtained in sixty-one cases, electrocardiographic examinations having been made in fifty-nine, and polygraphic tracings in two. The most frequent abnormality detected was prolongation of auriculoventricular conduction time (P-R interval 0.21 to 0.36 seconds), having been noted ten times,—in each instance in an active case. Changes in the ventricular complex (QRST) were uncommon, having been discovered in four cases only. In three of these, the alterations were inconspicuous and consisted of slight notching and widening of the QRS complex. In the fourth, the electrocardiogram showed the deviations characteristic of partial bundle-branch block. Necroscopic examination in this case revealed an aneurysm of the sinus of Valsalva caused by the

*The percentage of positive blood cultures is smaller than in the group reported by Libman and Celler[6] in 1910. The chief reason appears to be the fact that the cultures in the present series were not made by a single group of workers, but by a succession of laboratory assistants.

spread of the bacterial infection from the aortic valve to the root of the aorta. This aneurysm had projected into the interventricular septum in the region of the junctional tissues, and in serial sections it was determined that it had partially intercepted the path of the left branch of the bundle of His.

Alterations in the T-wave were noted several times, but the influence of digitalis therapy could not be excluded. The infrequency of alterations in the contour of the ventricular portion of the electrocardiogram contrasts sharply with its frequency in rheumatic fever (v. infra). Premature contractions (auricular, nodal, bundle, or ventricular) were recorded in six cases. Auricular fibrillation was encountered four times and auricular flutter once among the electrocardiographed cases, and there was no evidence that either of these arrhythmias was present in any of the sixty-two cases in which no electrical examinations were made. In one of the cases with fibrillation, the rhythm had been normal until three days before exitus. The blood culture was negative, but at autopsy numerous bacteria were found in sections of the endocardial vegetations. This is the only instance in the group in which fibrillation developed in an active case.* The notable fact is that the remaining three cases with auricular fibrillation and the one with flutter were proved at necropsy to be examples of subacute bacterial endocarditis in the bacteria-free stage.

If we exclude respiratory arrhythmia and occasional extrasystoles, it is of interest to note that the physical examinations revealed regular rhythm in all but five cases of the total number of 123. Four of these five were the patients with auricular fibrillation previously mentioned, and the fifth, a case with positive blood cultures, owed the irregularity of her pulse to a succession of extrasystoles.

Although it is possible for an occasional patient suffering from the active form of subacute bacterial endocarditis to develop fibrillation, these observations clearly indicate that this arrhythmia is not a part of the clinical picture of the disease. Even in the presence of heart failure these patients generally retain normal rhythm. Mason[7] reported the occurrence of paroxysmal attacks of auricular fibrillation in a case of subacute Streptococcus endocarditis, but it is doubtful whether this type of fibrillation is much more common than the permanent form. None of our patients gave a history of paroxysmal fibrillation.

The inquiry was approached from another angle by searching for evidences of active subacute bacterial endocarditis in a group of

*Since these observations were made, a number of additional cases of subacute bacterial endocarditis have been studied. One of these patients had auricular fibrillation, though the blood culture proved to be positive. The clinical picture, however, was complicated by the presence of Graves' disease, a condition which is itself frequently accompanied by fibrillation.

200 cases of auricular fibrillation. A large number had valvular defects due to antecedent rheumatic disease, the age incidence being about the same as the patients with subacute bacterial endocarditis, and the period of observation, which was one to ten years, sufficiently long to warrant conclusions; yet none of these patients had, when first seen, nor subsequently developed, subacute bacterial endocarditis. On the other hand, the occurrence of auricular fibrillation (or flutter) four times in fourteen cases of subacute bacterial endocarditis in the bacteria-free stage, shows that these arrhythmias are not infrequent during this stage of the disease.

Examination of the myocardium in subacute bacterial endocarditis discloses in the majority of cases focal lesions consisting of cellular infiltrations (chiefly of round cells) in areas where the muscle fibers have undergone degeneration or necrosis. These are the so-called Bracht-Waechter lesions which differ from the Aschoff bodies in certain essential particulars. They are frequently inconspicuous in size and distribution, but at times they are widely diffused throughout the myocardium, and the individual lesions may assume considerable proportions. Though they are situated mainly in the ventricular musculature, the infrequency of changes in the ventricular form of the electrocardiogram necessitates the assumption that they are generally without significant effect upon intraventricular conduction.

ELECTROCARDIOGRAPHIC FINDINGS IN RHEUMATIC FEVER

Directing our attention to rheumatic fever, it is well known that disturbances in the cardiac mechanism are common in this disease. The most frequent disorder which has been described is transient auriculoventricular heart-block, including all of its stages—prolongation of the P-R or a-c interval, dropped ventricular contractions, and partial or, in rare instances, complete auriculoventricular dissociation. Acute heart-block may in fact be the first sign of the disease. Other derangements of the heart rhythm have also been noted, including premature contractions of auricular, auriculoventricular, or ventricular origin, paroxysmal tachycardia, auricular fibrillation and flutter, nodal rhythm, sinus arrhythmia, and sinoauricular block. Parkinson, Gosse and Gunson[8] made a study of these disturbances in acute rheumatic fever, and summarized the previously recorded observations. More recently Cohn and Swift[9] made an exhaustive investigation in a series of cases and added an electrocardiographic sign of importance. They were able to show that the heart was affected in one way or another in thirty-five of their thirty-seven cases. Other recent studies are those of Bezançon and Weil,[10] Doumer,[11] and Bain and Hamilton.[12]

Our studies were begun in 1921. Sixty-five consecutive cases of acute rheumatic fever were investigated. Twenty-nine of the patients were admitted to the hospital during their first attack of rheumatic

fever. Twenty-four of these developed signs of endocarditis under observation, the mitral valve having been involved in each case, and in a small percentage the aortic valve as well. Thirty-one cases had definite signs of valvular disease on admission, and all of these gave a history of previous rheumatic infection. The remaining five were free of demonstrable disease of the heart valves, but displayed definite

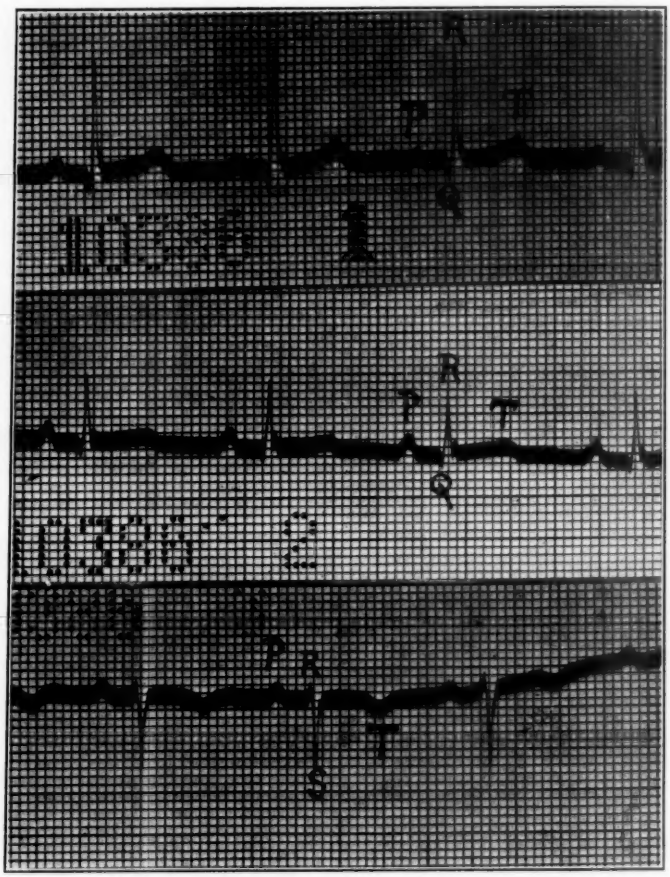

Fig. 1.—I. S., male, twenty-eight years old, was admitted to the hospital in November, 1926. The first attack of acute rheumatic fever began seven days before admission. The fever lasted three weeks. A systolic murmur over the apex and pulmonary area developed under observation. He was discharged symptom-free, January 31, 1927.

Electrocardiogram (10386): Left ventricular preponderance. P-R interval 0.16 of a second. Descending limb of R-wave in Leads I and II does not reach base line, and the T-wave appears to be given off directly from the R-wave. In Lead III the T-wave is inverted.

evidence of myocardial involvement. Electrocardiograms were taken weekly or oftener. Disturbances of conduction and of rhythm would unquestionably have been detected with greater frequency had examinations been made as often as in Cohn and Swift's series, but our

findings give valuable information concerning the changes which may be discovered in the course of routine electrocardiographic examinations of patients suffering from this disease. In each instance attention was directed to the occurrence of irregularities in rhythm, alterations in the length of the P-R interval, and modifications in the con-

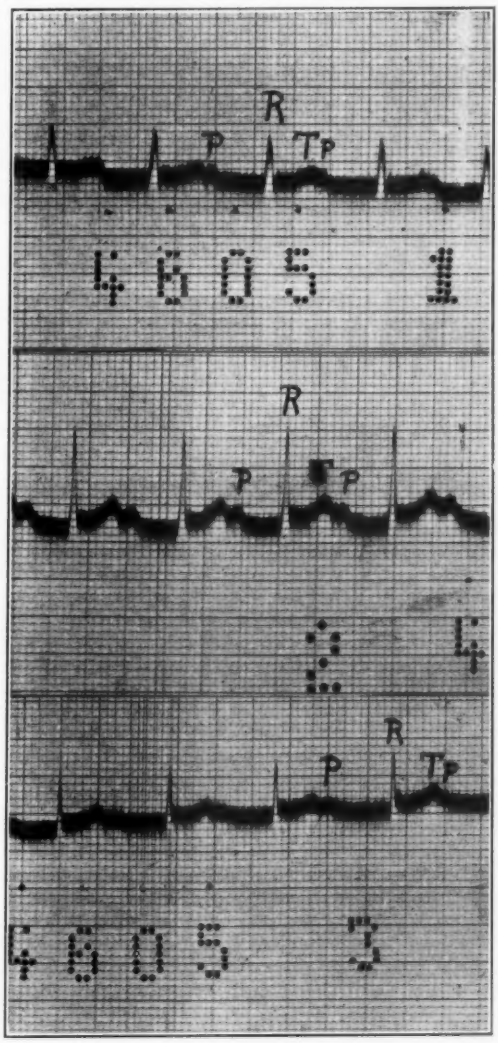

Fig. 2-A.—D. C., male, twenty-four years old, was first admitted to the hospital December 4, 1922. He had tonsillitis, peritonsillar abscess, and mild joint pains in 1920. Pain in the knees and chest began five days before admission to the hospital, and three days later he suffered from excessive sweating, fever, and dyspnea.

Diagnosis: Rheumatic fever; mitral stenosis and insufficiency; signs of aortic insufficiency developed under observation.

He was discharged January 10, 1923 and admitted again January 13, 1923 with complaint of dyspnea, weakness, and precordial distress. He was discharged Feb. 5, 1923.

Electrocardiogram (4605): Dec. 6, 1922, P-R interval 0.28 second. Loss of isoelectric period. R-T segment above base line.

tour of the ventricular complex. Other abnormalities in the electrocardiographic tracings were recorded when noted.

Delay in auriculoventricular conduction (P-R interval 0.20 second or over) was present in twenty-three of the cases (Fig. 2). In five of

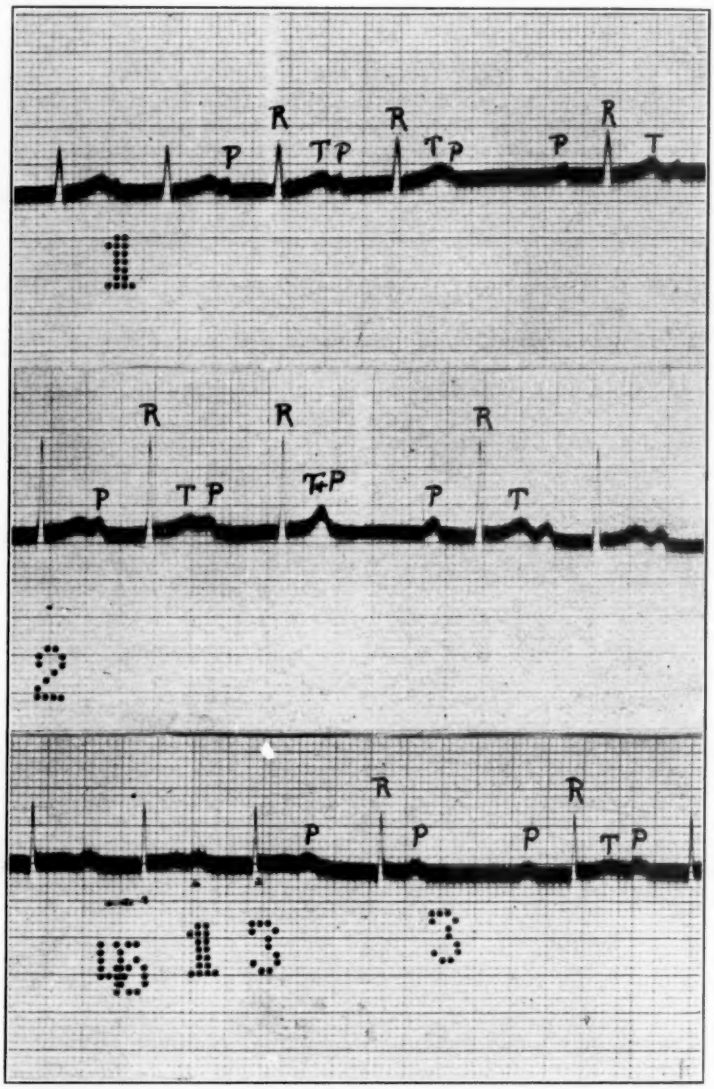

Fig. 2-*B*.—Electrocardiogram (4613): Dec. 11, 1922. Progressive lengthening of P-R interval with dropping of a beat. R-T segment somewhat above base line in Leads II and III.

these patients the defect of conduction had progressed to the stage of dropped ventricular contractions (Fig. 2) or incomplete auriculoventricular dissociation. Swift[13] found increased P-R time in 70 of 81 cases (86.4 per cent).

Changes in the form of the ventricular portion of the electrocardiogram (QRST waves) were frequent and proved to be even more characteristic of rheumatic fever than the impairment of auriculoventric-

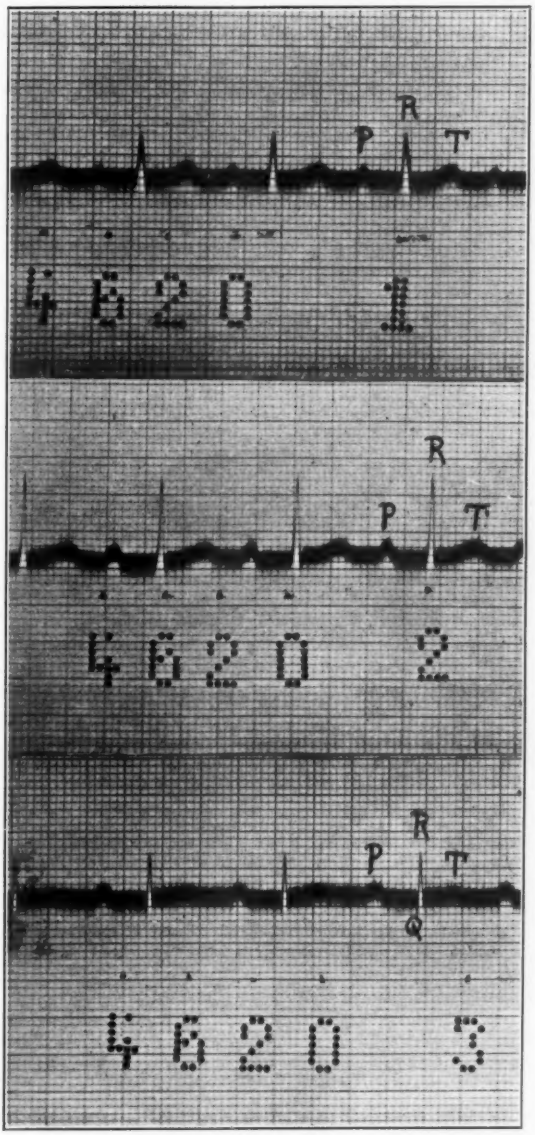

Fig. 2-*C*.—Electrocardiogram (4620): Dec. 13, 1922. P-R interval 0.28 second.

ular conductivity. They were recorded in 52 of the 65 cases or in 80 per cent, and were of three general kinds: those affecting the QRS complex, the S-T or R-T period, or the T-wave. The distribution of these alterations was as follows: The QRS complex alone was modi-

fied in five cases, the QRS complex and R-T or S-T segment together in fourteen, the entire QRST complex (including the T-wave) in sixteen, the S-T or R-T segment alone in eight, the S-T or R-T segment and T-wave combined in seven, and the T-wave alone in two. The

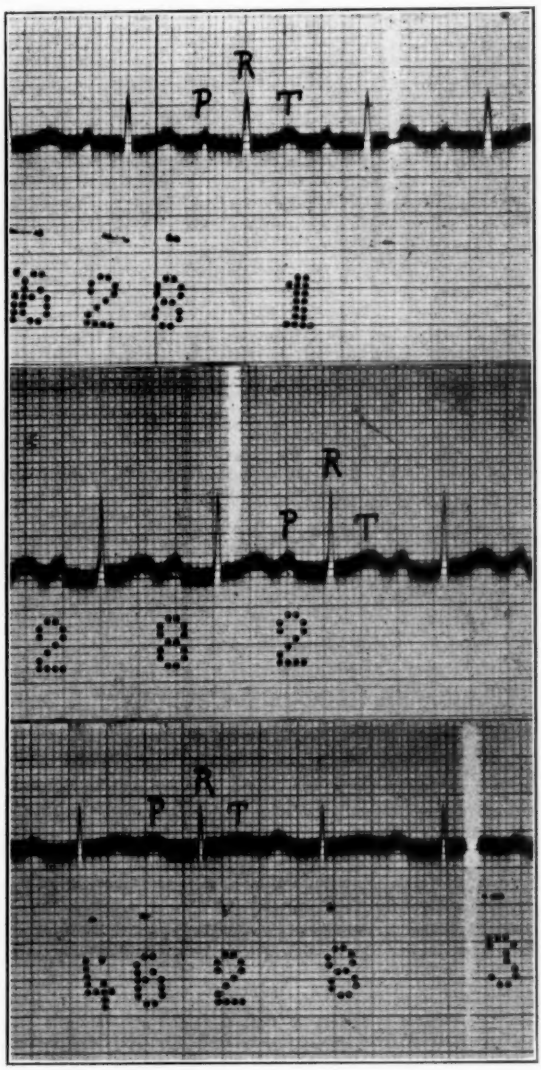

Fig. 2-*D*.—Electrocardiogram (4628): Dec. 18, 1922. P-R interval 0.24 to 0.28 second.

changes in the QRS complex were encountered either alone or in combination thirty-five times, but they were not conspicuous and consisted mainly of alterations in the amplitude of the R or S-wave, divergences in the direction of the waves, and notching and widening.

The changes in the R-T or S-T segment were more distinctive.

Normally, the foot points of the ascending and descending limbs of the R-wave lie at approximately the same level. After the downstroke of the R-wave reaches the base line, there follows a short interval before the T-wave begins, during which the galvanometric string is either quiescent or records a slow rise in the curve. This

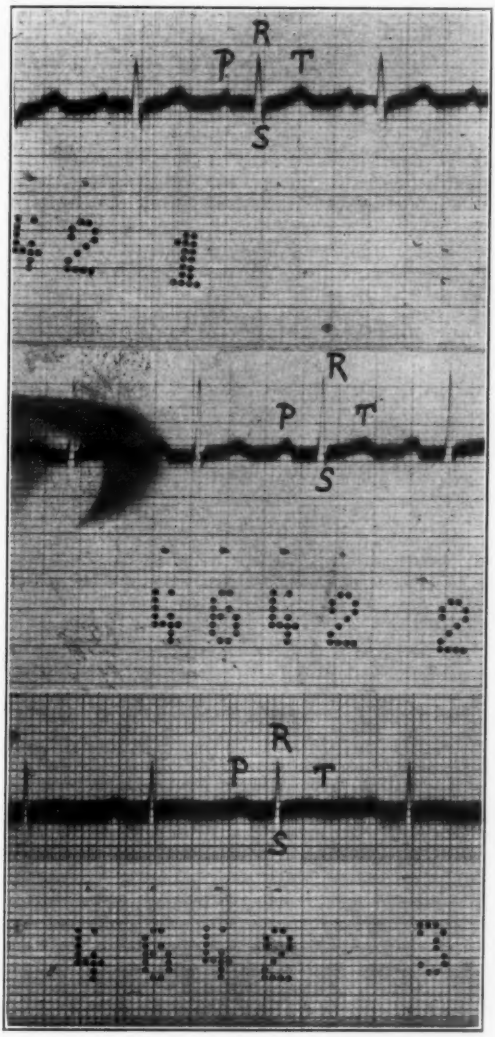

Fig. 2-*E*.—Electrocardiogram (4642): Dec. 27, 1922. P-R interval 0.20 second.

segment is the R-T period or, when an S-wave is present, the S-T period. Cohn and Swift[9] and we* found that alterations in this portion of the curve are frequently encountered in rheumatic fever. One of

*Our findings in 25 cases were presented briefly in the discussion which followed Cohn and Swift's paper before the American Society for Clinical Investigation, May, 1923.

the significant deviations is that which occurs when the downstroke of the R-wave fails to reach the base line and initiates an upward curve, occupying the whole of the R-T period, which becomes incor-

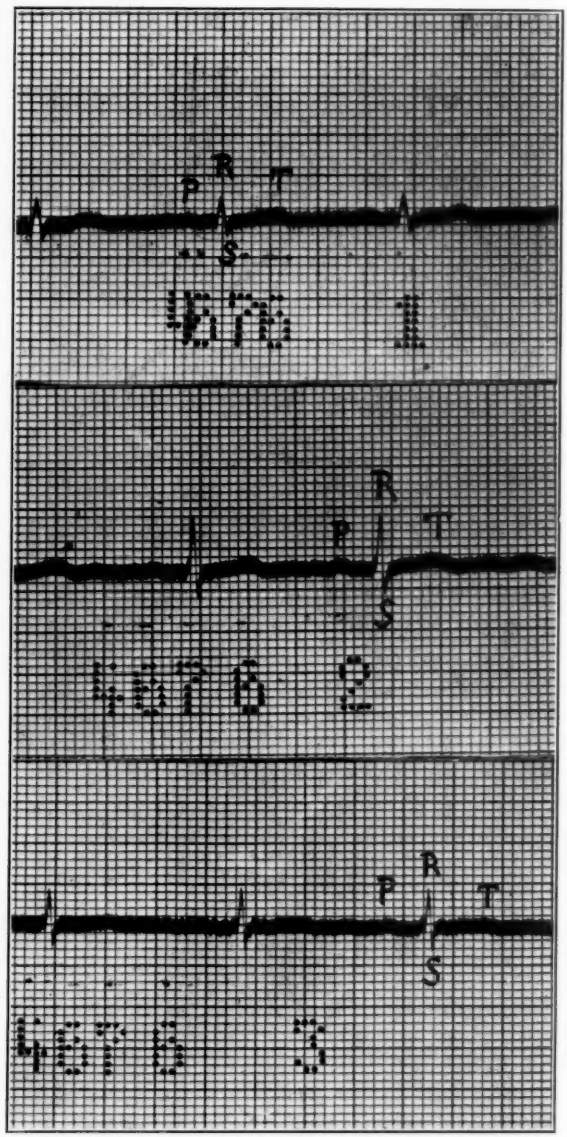

Fig. 2-*F*.—Electrocardiogram (4676): Jan. 15, 1923. Low voltage in Lead I, otherwise normal.

porated in the upstroke of the T-wave, so that it appears that the latter is given off directly from the R-wave (Figs. 1 and 2). In other instances, the descending limb of the R-wave may reach its normal position, or even extend below the base line to form an S-wave, but

the R-T segment, instead of occupying an almost horizontal position, may slope upward or downward to an unnatural degree. At times, the abnormal direction of the R-T or S-T period may continue after the anticipated beginning of the T-wave, so that the two portions become fused into a single wave. An alteration which is of a related kind was described by Cohn and Swift,[9] but was not encountered in our series. In this instance, the prominent phase of the QRS complex was the S-wave. The upstroke of the latter rose above the level of the foot piece of the ascending limb of the R-wave so that the S-T segment occupied a level which was conspicuously higher than that of the P-R interval. Alterations in the R-T or S-T segment either alone or in combination occurred in 45 per cent of our cases. The changes in the T-wave were mainly those of depression or inversion (Fig. 3), and were noted either alone or accompanied by other deviations in twenty-five cases.

The form of the ventricular portion of the electrocardiogram of a given individual is strikingly constant when studied over fairly long periods of time. Deviations in the contour of the various elements of the QRST complex may be regarded as evidence that the heart has sustained some functional or organic injury. The disturbances of auriculoventricular conduction and the irregularities in rhythm also denote myocardial impairment. If all the observed changes are taken into account, we find that the heart was affected by the rheumatic infection in 61 of our 65 cases (93.8 per cent).

The electrocardiographic signs of a given patient may undergo frequent changes during the course of the illness (Figs. 1 and 3). The duration of these alterations varied in our cases from three days to six weeks. Though the electrical disturbances are usually transient, we do not know whether they signified that the heart has suffered permanent damage.*

Impairment of auriculoventricular conductivity has been reported in influenza, pneumonia, diphtheria and typhoid fever, but in none of these conditions does it occur with the same frequency as in acute rheumatic fever. Certain drugs are known to prolong the P-R interval, but among these digitalis is the only one that is likely to lead to error. In the series of cases here reported digitalis was not responsible for the alterations observed. The changes in the form of the ventricular portion of the electrocardiogram also are not specific for rheumatic fever. Conspicuous deformities in the R-T segment have been reported in myocardial infarction due to coronary occlusion,[14, 15, 16] and less prominent changes have been noted in uremia,[17]

*Occasionally one encounters permanent heart-block due to cicatricial lesions of the auriculoventricular node or bundle resulting from antecedent rheumatic inflammation. In a subsequent communication, we shall report an electrocardiographic study of a series of cases of rheumatic heart disease, exhibiting permanent disorders of auriculoventricular or intraventricular conduction. This report will include the five cases of rheumatic myocarditis without accompanying valvular disease mentioned on page 360.

but it is clear that these are conditions which are not likely to be confused with rheumatic fever. Neither in them nor in any known infectious disease do changes in the latter part of the ventricular complex occur with such frequency as in rheumatic fever.

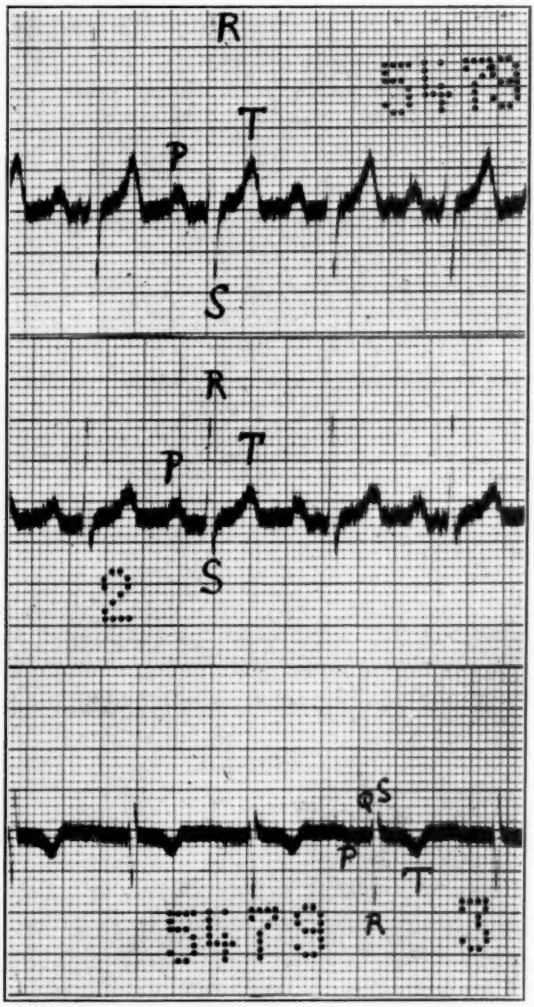

Fig. 3-A.—D. A., male, twenty-nine years old, had the first attack of rheumatic fever in 1916 and a second in 1919. He had a tonsillectomy in 1919. He had a third attack of rheumatic fever in November, 1923, and was admitted to the hospital Nov. 23. No murmurs were heard on admission; systolic murmur was first heard Dec. 10, 1923, and it disappeared Jan. 17, 1924. He had fever for two weeks after admission, and was discharged Jan. 29, 1924.

Electrocardiogram (5479): November 24, 1923. Left ventricular preponderance. Simple tachycardia. T-wave negative in Lead III.

Whether the disturbances in the mechanism of the heart are due to structural change or to toxic injury is difficult to state with certainty in the present state of our knowledge. It would be attractive to attribute the observed changes in conduction to the presence of the

specific lesions of rheumatic fever,—the submiliary myocardial nodules of Aschoff.[18] The transiency of the electrocardiographic alterations would go hand in hand with the ephemeral character of these

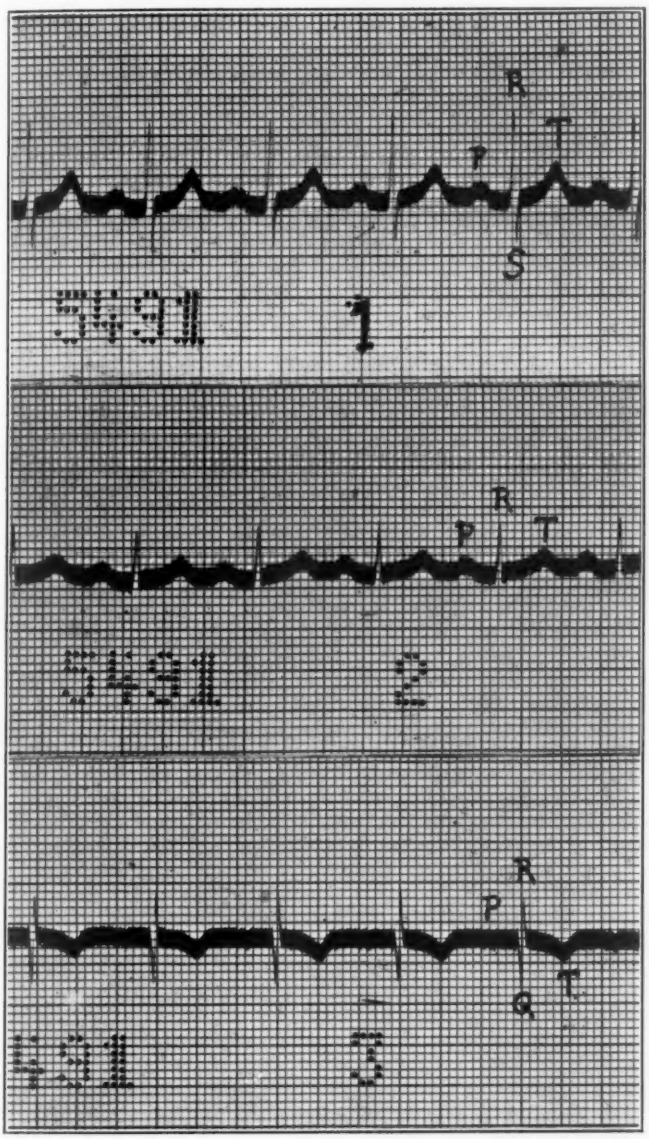

Fig. 3-*B*.—Electrocardiogram (5491): Nov. 27, 1923. Left ventricular preponderance. T-wave negative in Lead III.

lesions. The close proximity of the subendocardial Aschoff bodies to the fibers of the Purkinje system, the widespread occurrence of these lesions elsewhere in the myocardium,* the effects of collateral edema,

*In a few fatal cases of rheumatic fever with heart-block, acute inflammatory changes of a rheumatic kind were discovered in and about the auriculoventricular bundle.[19, 20, 21]

and local ischemias resulting from lesions in the coronary arterioles might be invoked to explain the electrical changes. When the Aschoff bodies are abundant this explanation may apply; but on the other

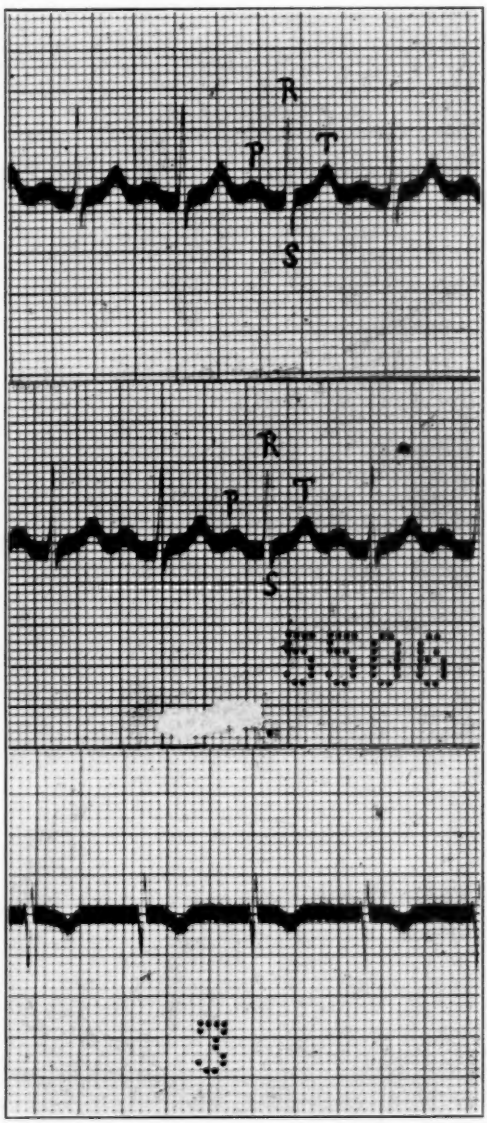

Fig. 3-*C*.—Electrocardiogram (5506): Nov. 30, 1922. Left ventricular preponderance. Simple tachycardia. T-wave negative in Lead III.

hand, our investigations of the pathological findings in rheumatic hearts have convinced us that Aschoff bodies are by no means present in every case of fatal rheumatic fever, even when the endocardial or pericardial inflammation is extensive.[17, 22] The electrocardiographic

signs are found much more frequently than the specific lesions, and when the latter are present, their number is often too small to account for the functional changes, so that for the present a definite correlation is not possible.

SUBACUTE BACTERIAL ENDOCARDITIS AND RHEUMATIC FEVER COMPARED

Comparing the findings in acute rheumatic fever with those observed in subacute bacterial endocarditis, we note that changes in the form of the ventricular portion of the electrocardiogram are far more common in the former than in the latter. This difference is particularly notable with respect to the R-T segment, in which alterations are so frequent in the one and so infrequent in the other. Prolongation of the P-R interval occurs in both, but decidedly more often in rheumatic fever, and the more advanced grades of heart-block are also more common in the latter disease. We have seen how rarely auricular fibrillation or the related arrhythmia, auricular flutter, is encountered in active cases of subacute bacterial endocarditis. Though valvular disease due to antecedent or chronic rheumatic infection is so frequently accompanied by auricular fibrillation, this arrhythmia is comparatively infrequent during the acute phase of the disease. Cases have been reported by Mackenzie,[23] Levine,[24] Laubry and Doumer,[25] Cohn and Swift,[9] Coombs,[26] and others, and one example was encountered in our series. The fibrillation has frequently been of the paroxysmal type.

CLINICAL CONSIDERATIONS

Though the electrocardiographic alterations recorded in acute rheumatic fever are not pathognomonic, they can frequently be employed as diagnostic aids. The following illustrative case may be cited. A young man was admitted to the hospital with fever, rapid and irregular pulse, and a red beefy-looking throat, but without joint symptoms. There was no previous history of arthritis. The heart was not enlarged, and there were no murmurs. Leucocytosis of moderate degree was found, and a blood culture proved negative. Because the electrocardiogram showed pronounced changes in its ventricular portion, acute rheumatic fever was suspected. It was not until five days later that the patient developed typical rheumatic arthritis.

There are cases in which the joints are entirely spared, the heart alone being affected. The inflammation may in fact be confined to the myocardium. When endocarditis and myocarditis coexist, the heart valves may give no signs for a long time. The presence of heart-block or changes in the ventricular complex will often give the first clue to the presence of rheumatic infection. On the other hand, there are cases of acute polyarthritis without clinical evidence of cardiac

impairment or other signs of rheumatic infection and the decision must be made whether the articular inflammation is rheumatic or nonrheumatic. In such instances, too, if other methods fail, the electrocardiographic examination may at times assist in making the differentiation. In five cases of acute polyarthritis which differed clinically from the rheumatic form, the electrical tracings exhibited none of the alterations noted in rheumatic fever. Though this series is too small to warrant final conclusions, the evidence offered is more than suggestive.

From time to time, one encounters cases in which it is difficult to distinguish between rheumatic infection and subacute bacterial endocarditis. The presence of the anhemolytic streptococcus in the circulation in rheumatic fever may lead to a mistaken diagnosis of subacute bacterial endocarditis. On the other hand, mild cases of the latter disease are known to exist,[27, 28] and their differentiation from rheumatic fever may sometimes present difficulties. A careful search for the signs of subacute bacterial endocarditis may reveal the presence of this disease. On the other hand, the existence of typical rheumatic polyarthritis (with redness and swelling of the affected joints), acute pericarditis, subcutaneous fibroid nodules, chorea or erythema gyratum (annulare), coupled with the absence of the characteristic symptoms of subacute bacterial endocarditis, would point to the diagnosis of rheumatic fever. It is necessary to rely chiefly upon the clinical findings in the discrimination of these conditions, but in equivocal cases it is suggested that the clinical study be supplemented by electrocardiographic examinations. Definite changes in the ventricular complex, especially in the R-T or S-T segment, would suggest rheumatic infection.

The knowledge gained in this investigation that the heart is implicated in almost every case of rheumatic fever has been of service to us in determining how long to keep the patient in bed. For several years, it has been our practice not to allow patients showing the electrocardiographic changes to leave their beds until the tracings have resumed their normal appearance.

The observations upon the heart rhythm in subacute bacterial endocarditis too have permitted us to draw certain diagnostic conclusions. Given a patient with valvular disease and persistent fibrillation, it is not likely that active subacute bacterial endocarditis is present. This is true even in the presence of fever and embolic phenomena, for the fever in such cases will generally be found to be due to extracardiac causes, e.g., pneumonia or to an unrecognized chronic rheumatic infection,[29] and the embolism to a thrombus in the left auricle. If the more distinctive signs of subacute bacterial endocarditis, i.e., petechiae with pale centers, Osler nodes, splenomegaly, clubbing of the fingers, nephritis, sternal tenderness, facial pigmentation, are discov-

ered in a patient with persistent fibrillation, the diagnosis will often prove to be subacute bacterial endocarditis in the bacteria-free stage.

The observation that subacute bacterial endocarditis is not likely to develop in patients with chronic valvular disease after the onset of fibrillation is similar to another of a related kind, namely, that individuals with severe cardiac failure, conspicuous lesions of the tricuspid valve, or pronounced stenosis of the mitral valve enjoy a high degree of immunity to this disease. Cardiac insufficiency can, of course, supervene after bacterial infection of the valves has developed, especially in the healing or healed stage.

SUMMARY

The rhythm of the heart was investigated in 123 cases of subacute bacterial endocarditis, 109 of which were in the active or bacterial phase of the disease, and 14 in the bacteria-free or healed stage. Auricular fibrillation was encountered but once among the active group, an incidence of less than 1 per cent, and in this case the rhythm had been normal until three days before death. In three other cases in which fibrillation was noted and in the single instance of flutter, the endocarditis had already progressed to the bacteria-free stage. These findings demonstrate how exceptional auricular fibrillation is in the active or bacterial period of the disease. On the other hand, this irregularity is observed in the bacteria-free stage with perhaps the same frequency as in chronic rheumatic valvular disease. Observations upon a large series of patients with fibrillation have convinced us that once this arrhythmia is permanently established, there is little danger that subacute bacterial endocarditis will supervene. The observation that auricular fibrillation and active subacute bacterial endocarditis are mutually exclusive (save in an exceptional instance) is of diagnostic value.

Depression of auriculoventricular conductivity as manifested by prolongation of the P-R interval was noted a number of times in subacute bacterial endocarditis, but in a much smaller percentage than in cases of rheumatic fever. A more conspicuous difference between the two diseases lay in the comparative incidence of alterations in the ventricular portion of the electrocardiogram. The characteristic changes particularly of the R-T or S-T segment proved more frequent in rheumatic fever than in any other known febrile condition, including subacute bacterial endocarditis.

If we include as evidence of myocardial injury not only prolongation of the auriculoventricular conduction time, and alterations in the contour of the ventricular portion of the electrocardiogram, but also the irregularities of heart rhythm noted, our findings indicate that the heart was involved in 61 of the 65 cases of rheumatic fever investigated. The electrical changes were found to vary within wide lim-

its during relatively short periods of time and in most instances disappeared. Though these changes were usually transient, we do not know as yet whether their presence denotes that the heart has suffered permanent damage. These observations are of importance first, because they demonstrate that the myocardium is implicated in some way in almost every case of rheumatic fever, and second, because the electrocardiographic signs furnish a means of detecting cardiac invasion when other signs are wanting. Judiciously correlated with the general clinical study, these electrical changes will be found to be of diagnostic value.

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SOME MODES OF INFECTION IN RHEUMATIC FEVER*

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MOST writers agree that, as a rule, children, sick in hospitals with rheumatic heart disease, are not retained as institutional patients for periods of time long enough to ensure their complete recovery. At Montefiore Hospital children with rheumatic heart disease are kept in the children's wards for many months at a time, so we have thought it worth while to review a series of cases that have received prolonged institutional treatment to discover what benefits, if any, may be ascribed to their institutional residence. With this point in view, we have studied the records of fifty-three children under fifteen years of age with rheumatic heart disease, who were patients in Montefiore Hospital between May, 1921, and May, 1926. This survey was provoked by the impression we had gained that, in spite of the fact that these children were living in an environment supposedly far more favorable than that offered by their own homes, reinfections were rather frequent and often of serious import.

All of these children had, on admission, organic valvular lesions, resulting from previous rheumatic infection. Most of them had been ill for varying periods of time either at other hospitals or at home and were admitted to our institution for further medical attention and observation. Many of them had no history or signs of congestive heart failure and were up and about, well enough to attend the hospital school. Others showed varying degrees of cardiac insufficiency. Some were febrile on admission, others were not. Of the fifty-three children, thirty-eight were boys and fifteen girls. The average age of the boys was eleven years and of the girls eleven and six-tenths years. In the whole series the ages ranged between six and fifteen years. The average stay in the hospital was 277 days, the period of institutional residence ranging from twenty-five days to three years.

Thirty-nine, or almost three-quarters of the fifty-three patients, experienced febrile episodes, the temperature during the attacks varying from 99.6° to 105°, and lasting from one day to over eight months. Twenty-six of these children were males, and thirteen were females. The thirty-nine patients had sixty-three bouts of fever in all. The remaining fourteen patients were afebrile throughout their entire stay

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in the hospital. The presenting lesions associated with the rises in temperature were as follows:

	No. of cases
Pericarditis	8
Arthritis	2
Tonsillitis	10
Pharyngitis	6
Bronchitis	6
Bronchopneumonia	5
Rheumatic fever	21
Constipation	3
Alveolar abscess	1
Otitis media	1
Total	63

Fourteen of the children presenting febrile bouts died while under observation. Of these, ten showed signs of active rheumatic fever at the time of death. Three died from bronchopneumonia, while only one succumbed to heart failure following a prolonged period of decompensation with auricular fibrillation. Eleven of the fourteen cases showed at the time of death clinical evidences of pericardial involvement.

The significance of febrile episodes in children is often hard to evaluate. In particular, the diagnosis of rheumatic fever in a child with organic heart disease is very difficult. Acute articular rheumatism is uncommon in children, and only two of the children of our series exhibited acute arthritis. At times fleeting joint or muscle pains, or an evanescent pericardial rub, may be the only rheumatic manifestation, or the appearance of a crop of subcutaneous nodules may offer a clue. More often the diagnosis must be made by eliminating every other possible cause of fever, and noting tachycardia disproportionate to the fever, a rise in the neutrophil count, and more particularly the rapid appearance of a marked secondary anemia. Again electrocardiographic changes, such as changes in the ventricular complexes or prolongation of the P-R interval, as reported by Cohn and Swift[1] may give evidence of an acute inflammatory process in the heart muscle. We have taken fifty electrocardiographic records of thirteen children during bouts of rheumatic fever, although only three of them are included in this series, and in only three have we been able to register any changes in the electrocardiogram. One showed premature contractions and two showed partial heart-block.

Of the sixty-three febrile episodes, thirty-one were certainly manifestations of rheumatic fever. In eight there was pericarditis, in two arthritis. In twenty-one the diagnostic criteria were the general ones

enumerated above. In a certain number of instances attacks of tonsillitis and pharyngitis, sixteen in all, were certainly related to rheumatic infection.

The significance of bronchopneumonia and bronchitis and their relation to rheumatic fever in these children is not easy to determine. Although rheumatic pneumonia has been described by several authors, most recently by Rabinowitz,[2] the evidence for a specific etiology of these lung infections is not at all convincing. In 1845 Latham[3] had noted a frequent coincidence of pulmonary inflammation with inflammation of the heart in patients with acute rheumatism. Some of our observations suggest a very close relationship between certain instances of pulmonary infection and rheumatic fever, although we cannot state with certainty whether this infection was actually caused by the rheumatic virus, or whether it was merely a predisposing factor, either facilitating its entrance into the body, or reactivating a latent lesion. In seven of the cases of this series the bout of rheumatic fever was ushered in by a bronchopneumonia, and in these children it was impossible to know when the bronchopneumonia ceased and when the rheumatism began. The two conditions merged insensibly one into the other. Furthermore, we noted, as will be described in greater detail below, that during the period of a ward infection, one child would have bronchopneumonia, another carditis, another pericarditis. Indeed, the severest ward infection began with two cases of bronchopneumonia. One of these cases we wish to report in full, in view of the fact that the necropsy demonstrated the specific lesions of rheumatic fever.

S. W., (History No. 13521), a boy aged thirteen years, was admitted to the hospital on August 30, 1925. He had had an attack of acute articular rheumatism two years prior to admission. In March, 1925, he had an appendectomy performed and two weeks later developed bronchopneumonia. During the subsidence of his lung infection, most of his large joints became swollen, red, tender and painful. It was at this time that his physicians discovered a valvular heart lesion. After a stormy convalescence of about four months, he recovered sufficiently to be up and about. Physical examination on admission revealed a heart greatly enlarged, particularly in the region of the left ventricle, with aortic insufficiency and mitral stenosis and insufficiency. During the first six months of his stay in the hospital he was up and about and was able to attend the hospital school, and gained thirty-five pounds in weight. On March 3, 1926, during the ward epidemic, which will be described below, his temperature rose to 101°. The following day he complained of cramps in the lower abdomen, as well as shooting pains in the joints. Within two days the temperature rose to 104°, the abdominal pain continued, the respirations became rapid, and he coughed up rusty-tinged sputum. There were dulness and diminished breathing at the right base, the white cell count was 35,200 with 90 per cent polymorphonuclear cells. On March 8 premature beats were observed. On March 10 dulness and diminished breathing were noted at the left base. The temperature continued between 101° and 103° and on March 19 the presence of empyema was suspected, but exploratory chest puncture revealed no pus. On this day the white cell count was 19,200 with 74 per cent polymorphonuclears. The fever continued but became more

remittent. On March 26, roentgen examination showed poor areation of both lungs and small, irregular infiltrations in both lower lobes, which were interpreted as evidence of a resolving bronchopneumonia. The remittent fever continued and was accompanied by profuse sweats. The blood culture was negative. The heart rate became more rapid, remaining around 140° most of the time, even when the temperature was 101° and lower. On April 7, because of the persistent fever, very rapid heart rate, and the progressive anemia, the diagnosis of rheumatic carditis was made. On the following day his hemoglobin was 55 per cent, the white cell count was 28,800, with 81 per cent polymorphonuclears. A friction rub was heard in both chests, the heart gradually became more rapid and weaker, and the patient died on April 13, six weeks after the onset of his illness.

Necropsy, performed by Dr. D. P. Seecof, revealed a heart weighing 650 gm., with enlargement of both ventricles. The parietal and visceral layers of the pericardium were adherent all over the heart. The mitral leaflets were diffusely thickened and puckered, causing a moderate stenosis of the orifice. The aortic leaflets were thickened and shortened. Both mitral and aortic valves showed ridges of minute verrucous vegetations. A few discrete similar vegetations occurred on the tricuspid leaflets. The lungs showed dense pleuropericardial adhesions and many fibrous tags all over their surfaces. The lower lobes were rather firm and fleshy and exuded a large amount of serum, but exhibited no definite foci of bronchopneumonia. Microscopic examination revealed marked passive congestion with thickening of the alveolar walls, and in several sections an organizing pleuritis. Microscopic examination of the heart muscle showed many typical, well preserved Aschoff bodies.

Here, then, is a case beginning with fever and joint pains, followed within two days by bronchopneumonia, which was demonstrated radiographically. The pneumonia lasted many weeks and gradually the clinical picture became that of rheumatic carditis. At necropsy Aschoff bodies were found in the heart.

The condition of the patient on admission is to some extent a factor in determining the frequency of recurrent infections, as is shown in Table I, in which the patients are grouped in the classes suggested by the New York Heart Committee: I—able to carry on ordinary physical activity without discomfort; IIa—Activity slightly limited; IIb—Activity greatly limited; III—Unable to carry on any physical activity without discomfort.

TABLE I

CLASSIFICATION ON ADMISSION	I	IIa	IIb	III
Number of cases	12	22	9	10
Number reinfected	7	14	8	10

It seems that the children with the most advanced lesions are most susceptible to reinfection, or else are more apt to be harboring a smoldering infection.

Twenty of the thirty-nine children who showed rises in temperature during their hospital stay had had their tonsils removed prior to admission, while ten of the fourteen who remained afebrile had had tonsillectomies performed. Furthermore, it is of interest that only ten of the sixty-three bouts of fever exhibited by the thirty-nine pa-

tients were associated with actual tonsillitis. The tonsil, therefore, does not seem to be so important a portal of entry for rheumatic infection as is generally supposed, and tonsillectomy appears to be of little avail in reducing the hazards of reinfection.

We have been greatly concerned to discover, if possible, the cause of the frequency of reinfection in these children. Three-quarters of the children in our series experienced febrile episodes. Smith and Stulik[4] studied eighty children with rheumatic heart disease for three years in a dispensary and found that only one-quarter of them had periods of slight fever. Our experience in our dispensary class has been quite similar.

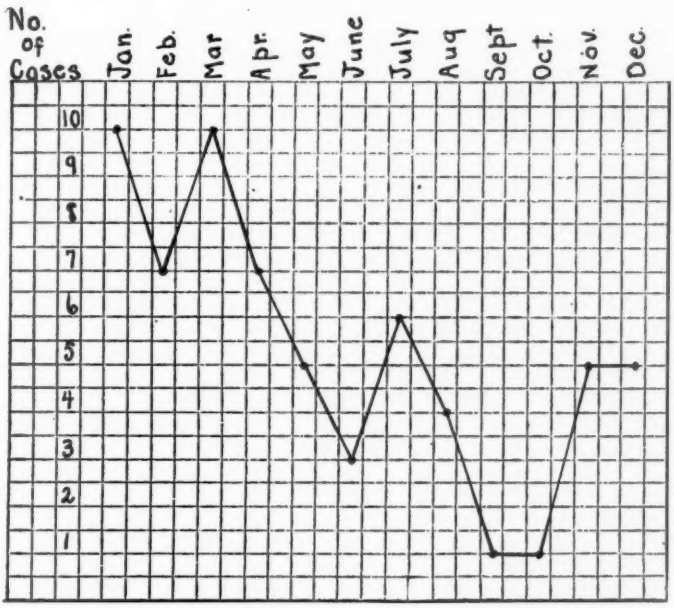

Fig. 1.—Seasonal distribution of the cases of rheumatic fever studied.

As is apparent from Fig. 1, there is a distinct seasonal variation in the incidence of rheumatic infection in our series, with the greatest number of infections occurring from November to March. This corresponds with the general seasonal distribution of rheumatic fever in New York City. There are no direct environmental factors that can be held responsible for the frequent infections. The children are housed in dry, sunny and airy wards. Their diet is wholesome and adequate, as evidenced by the fact that, in spite of their various illnesses, two-thirds of them gain in weight during their hospital residence.

There remains the possibility of contact infection. Although this is discounted by most physicians, a study of the distribution of the febrile bouts almost compels this conclusion. Indeed, twice in one

year there occurred what appeared to be ward epidemics and it is these which we wish to discuss in particular. Both epidemics occurred in a large boy's ward which houses eighteen children.

In February, 1926, there were in the ward eleven boys suffering from chronic rheumatic valvular heart disease, six ambulatory boys suffering from various neurological conditions, and one child with chronic tuberculous joint disease and amyloidosis. The rheumatic children had been afebrile for many weeks. On February 24 one of the boys developed fever and within two days showed evidence of a well-developed bronchopneumonia with subsequent signs of carditis. Seven days later, the child, whose protocol has been given in detail above, became ill with pneumonia followed by carditis, which was verified at necropsy. On March 16, a boy, whose bed was at the opposite end of the ward from those of the first two, became febrile and on the second day began complaining of severe precordial pain. Within a few days a pericardial friction rub was heard and a pericardial effusion developed. His cardiac infection ran a typical severe course and was accompanied by signs of bronchopneumonia. The consolidation of the lungs showed on the roentgen plate. He died on April 14. A week after the onset of the third case, a fourth boy began to run fever with a cough and the production of blood-tinged sputum. In his case, as in that of the first two, the signs at first were those of bronchopneumonia, which gradually merged into those of rheumatic carditis, the heart enlarged, the pulse rate remained rapid, and anemia developed. On March 31 another boy developed acute tonsillitis, which was accompanied by a blotchy purpuric eruption and followed by pyelitis. Fever and tachycardia lasted a month. These five children all had been admitted to the hospital with chronic rheumatic valvular disease but had apparently been free from infection for weeks preceding the onset of this epidemic. The remaining twelve children in the ward, of whom six were suffering with heart disease, escaped infection.

Following this epidemic the ward remained free from infection until the fall. On November 1 a renewed outbreak occurred, but again only in the boys with damaged hearts. On this day one of the boys developed a sore throat with fever, malaise, and general body pains. The fever continued over a period of many weeks, and the disease took the course of rheumatic carditis. During the third week the left knee became swollen and tender. Death occurred December 6. Autopsy revealed fresh verrucous vegetations on the mitral and aortic valves and Aschoff nodules in the myocardium. On November 14 another boy was seized with a fulminating infection with high fever, severe abdominal pain, showers of petechiae, and dropped beats were noted on auscultation at the apex. The blood culture was negative. The infection persisted nine weeks and resulted in his death. On

November 19 another boy became febrile, complained of pain in his hip, and exhibited signs of partial heart-block, which were verified electrocardiographically. He, too, ran a severe and prolonged course, which was complicated by signs of cardiac insufficiency. On the same day as the preceding case, another boy, who had recently recovered from a rheumatic infection, again developed fever which persisted for two weeks and was not accompanied by any localizing signs. On November 24 another child had a sudden elevation of temperature which persisted for three weeks without any definite localizing signs, but with tachycardia, leucocytosis and anemia. On November 30, a sixth boy showed fever and marked general urticaria, particularly of

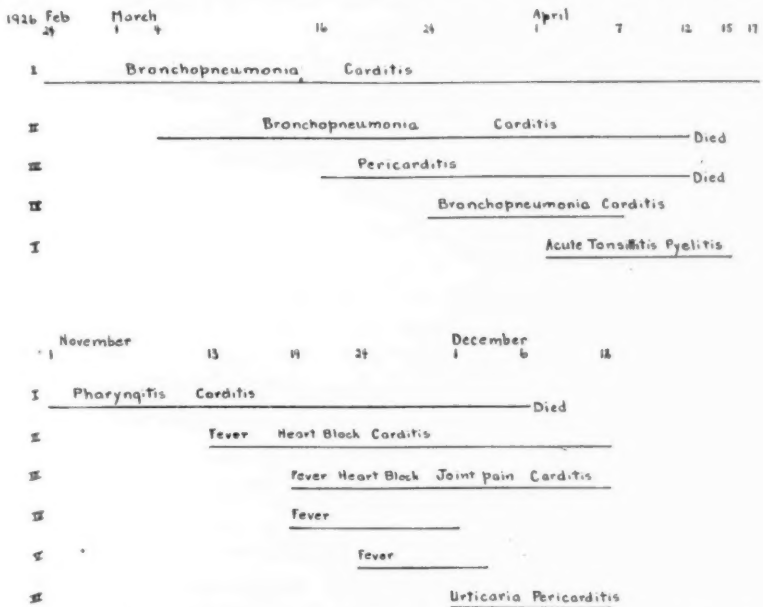

Fig. 2.—Course of two ward infections of rheumatic fever described in text.

the face. The urticaria disappeared within a few days but within a week a well-developed pericardial friction rub became audible which persisted for three weeks. During the period of this epidemic there were five children with chronic rheumatic valvular disease in the ward and thirteen others with miscellaneous medical and neurological conditions. None beyond those described above gave evidence of acute rheumatic infection.

We believe that any impartial observer will concede that the succession of cases that we have described constitute real ward infections or epidemics. No instances of acute rheumatic infection occurred in the girls' ward in the hospital during the periods of these epidemics, although there were six children with chronic rheumatic valvular disease there at the time. The question naturally arises were they epi-

demics of true rheumatic fever, or were they nonspecific infections which activated the rheumatic virus, latent in the several victims? This is most difficult to answer. In favor of the latter assumption is the fact that no cases developed among the nonrheumatic population. However, the onset with heart-block in two cases, with pericarditis in one, and with urticaria and pericarditis in another case, suggest strongly a primary rheumatic infection. It is quite rational to suppose that infection can occur only in susceptible individuals. Diseases vary in their degree of infectiveness; some, like measles, attack all who are exposed for the first time, others, like meningococcus meningitis or poliomyelitis, find many resistent individuals. It is very likely that with the discovery of the virus of rheumatic fever this apparent inconsistency will be explained.

There is much evidence in the literature supporting the view that rheumatic fever may partake of the nature of an epidemic disease and that contact infection is possible. Garrod[5] in 1890 showed that rheumatic infections vary in character from year to year. One year the cases are severe, another year they are mild; similarly, there are annual variations in the frequency of cardiac involvement. Newsholme,[6] in his classic paper on the epidemiology of rheumatic fever, said, "Death returns agree in manifesting very great irregularities in the yearly incidence of rheumatic fever, the excesses of prevalence in certain years being so great as to merit the name of 'epidemic.'" He further showed that there may be an explosive outbreak of cases. Thus, in its epidemicity, rheumatic fever resembles many infectious diseases.

A number of local epidemics have been described. In 1887 Feltkamp[7] described a ward infection similar to those we have observed. During the war Grenet[8] noted that rheumatic fever was confined to certain regiments. When the rheumatic troops moved to a new sector, cases of rheumatic fever appeared in the new contact troops; but the fresh regiment which occupied the abandoned quarters of the rheumatic regiment did not develop any cases of rheumatism. He also noted two instances of ward infection. Six days after the admission of a patient with rheumatic fever, two wounded soldiers in the same ward who had had no previous rheumatic disease, developed acute articular rheumatism. At another time a patient convalescing from pneumonia, who was exposed to a case of rheumatic fever, contracted the disease. Finally Herrmann[9] saw ten cases of rheumatic arthritis developed between May 1 and November 11, 1923, in a correctional institution which harbored one hundred and ninety boys. Five of the cases occurred between May 1 and July 8. He, however, endeavored to find an endemic factor to explain this series of cases.

Many instances of apparent contact infection have been reported. Mantle[10] saw a family in which the daughter developed erythema

nodosum following which her father, and then her mother, each a week apart, developed first attacks of articular rheumatism. He describes three other instances of contact infection. Meyer,[11] Josseran,[12] Monnier,[13] and Turner,[14] describe a number of similar instances. Talamon[15] and de Treigny[16] described cases of articular rheumatism occurring simultaneously in husband and wife. In each case only one partner had been previously subject to this infection. We have seen a similar instance of conjugal arthritis which was not due to gonorrheal infection. Hawthorne[17] treated a family in which rheumatism in one son was followed in a few days by a similar infection in another son. Seven days later a daughter became ill with articular rheumatism, and after three more days the father and a third son were taken with the disease. After another week a married sister, who had visited the sick family daily, was taken with acute rheumatism. Three instances of rheumatic fever in newborn infants, whose mothers were suffering from rheumatic fever at term have been reported.[18] Finally, St. Lawrence[19] and others[20] have shown that arthritis, chorea, and cardiac disease frequently occur in several members of one family. St. Lawrence found two or more cases of rheumatic infection in fifty of one hundred families of patients from his cardiac clinic, and suggested that these arose by contact infection. Twenty-eight years ago Cheadle made similar observations but interpreted them as indicating the strong hereditary factor in rheumatic fever.

In spite of our increasing knowledge of the nature of rheumatic fever, there is a persistent tendency to focus attention too exclusively on the heart, and too little on the systemic infection. It is true that the enthusiasm for the eradication of foci of infection in the tonsils and teeth has led toward a broader concept of the nature of rheumatic heart disease, but the results of these measures have been rather sterile in their benefits to patients and to the progress of knowledge. Today, when through the agencies of heart associations and cardiac clinics, there is such a widespread and laudable attempt to prevent and control the ravages of cardiac infection, and when the hope is expressed that through organized effort the mortality from heart disease may be reduced in the same degree as has the tuberculosis death rate in recent years, it is of fundamental importance to comprehend fully the significance of our broadening knowledge of the nature of rheumatic infection.

It has become more and more apparent that rheumatic fever is an infectious disease of great invasive powers which may produce lesions in many parts of the body. The heart is but one of many organs and tissues in which the virus may cause morbid processes. It is only because this vital organ is so indispensable to health and to life that the symptomatology and clinical interest of rheumatic fever are referred so predominatingly to the heart. It is not our purpose in this

paper to discuss at length the evidence supporting this view. This has been done admirably by Swift,[21] particularly from the clinical point of view, and by Sacks[22] from the pathological angle. We but wish to recall that the great variety of symptoms in rheumatic fever, such as pharyngitis, tonsillitis, chorea, arthritis, carditis, pleuritis, vague muscle pains, subcutaneous nodules, have their counterpart in pathological lesions equally widespread, and all conforming to the same general type of tissue reaction.

Furthermore, it is of importance to remember that in children the infection is generalized, with protean manifestations in the muscles, fasciae, tendons, joints, serous membranes, the respiratory tract, the brain, and the heart. In adults the infection is restricted more particularly to the upper respiratory tract, the joints and the heart; its manifestations are more sharply localized. A certain analogy has been drawn between rheumatic and tuberculous infection in children and in adults. In the very young infection with the tubercle bacillus results in the widespread lesions of miliary tuberculosis, usually with meningitis; in adults, as a rule, it becomes localized in the lungs, but at times in the bones, glands, joints, or urogenital system. Swift has drawn a similar analogy with syphilitic infection, contrasting the diffuse secondary stage with the more localized lesions of the tertiary period. It would seem that in all three diseases the varying forms of reaction of the body to infection are determined primarily by an acquired immunity which, in the case of rheumatism and tuberculosis, is lacking in the young, but acquired to a certain degree with advancing years.

The course of rheumatic fever in children differs furthermore from that of adults in its chronicity. Whereas, in adults reinfection is infrequent and the duration of each bout of arthritis or carditis is measured usually by a period of a few weeks, in children reinfection is the rule, and attacks lasting several months are not at all uncommon.

The failure of present-day efforts to prevent rheumatic heart disease is due not alone to our ignorance of the identity of the rheumatic virus and of its mode of entry into the body, but to a disregard of the known facts of the natural history of rheumatic infection, as well. Of what avail is tonsillectomy when the virus may persist in the heart, synovia, or subcutaneous nodule for months at a time, ever ready to give rise to reinfection? Of what avail are convalescent homes when they admit, to a large extent, children who are temporarily free from infection, and then only for a relatively short period of time? Of what avail are general hospitals when they discharge their patients with rheumatic fever before the infection is completely eradicated from the body?

The most hopeful suggestion in the present state of our knowledge first proposed by Raven[23] and echoed by Swift and others[24] is to pro-

vide sanatorium treatment for rheumatic subjects, quite analogous to that established for tuberculous patients. Here patients harboring rheumatic infection would be treated for periods of six to twelve months or longer under a strict sanatorium regimen, with the employment of all of the usual aids of rest, proper food, light and air, with a closely supervised resumption of the full activities of health.

SUMMARY

We have tried to show, both from our experience and from a survey of the literature, that rheumatic fever has many of the characteristics of other infectious diseases with a low degree of contagiousness, but that at times, and under special circumstances, it may assume epidemic proportions. We have pointed out the importance of the lungs as a source of reactivation or as a portal of entry of rheumatic infection, and have drawn attention to the close connection that exists at times between bronchopneumonia and rheumatic carditis. We have tried to reemphasize the importance of regarding rheumatic fever as a generalized systemic infection of great chronicity, and consequently the inadequacy of directing the attention too exclusively to one organ, such as the heart or the tonsils. We have shown the relatively minor rôle played by the tonsils as sources of reinfection. Finally, we have tried to indicate the inadequacy of present methods for after-care of children with rheumatic heart disease and the harmfulness of the ordinary form of prolonged general hospital care. The problem of the rheumatic child can be met only by providing some form of extended sanatorium treatment in an effort completely to eradicate the rheumatic virus from the infected individual.

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HEART DISEASE FROM THE POINT OF VIEW OF THE PUBLIC HEALTH*

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(*Continued from page* 301.)

IF WE return now to consider the etiological groups which have contributed to the total of deaths after age forty, the largest number of cases are due to senescence. A certain number are found to be sequels of syphilitic infection. There are included, also, a number of cases acquired at this age, of valvular heart disease, and perhaps of muscular disease too, due to rheumatism and to a lesser extent to other infectious diseases, and a certain number due to infection acquired before this period. Arrival at old age brings with it certain disadvantages. It not only ushers in the natural probability of death by a normal cardiac mechanism, but on account of the inherent defects of the system in advancing years, exposes individuals to injury, as Dublin[56] suggests, to which they were earlier not prone. Exactly which these might be from the point of view of the circulatory system is not yet quite clear. But if this system were so affected, a disease of old age, rather than old age itself, will have occurred; cases of this nature would perforce swell the cardiac death rate. But the overwhelming majority of cases must be due, if the considerations which have been urged are correct, to the cause just mentioned. It has already been

*From the Hospital of the Rockefeller Institute for Medical Research, New York. Delivered as a De Lamar Lecture at the School of Hygiene and Public Health, Johns Hopkins University, Baltimore, November 15, 1926.

shown that five-sixths of the deaths from heart disease occur after age forty. If these were due in large measure to muscular and vascular rather than to valvular diseases one would expect if the muscular diseases were separated to find a greater percentage of cases of this type after age forty. That this is actually a fact has already been shown (Table IV). Of 957 cases, 93.2 per cent were forty and over.

The duration of muscular disease of the heart has been studied by Romberg[30] in 176 cases in the Leipzig clinic. It was found there that the interval between the time when the first attack was experienced and when the heart began to fail averaged fourteen and one-half months. The time between the beginning of heart failure and death averaged five and one-half months, ranging from a few days to two to three years. On this basis the total duration is put down as one and one-half to two years, ranging from a few days to twenty years. Cases were known to last as long as ten to fourteen and even seventeen to twenty-three years.

That cases of syphilis also fall into this group, appears from the fact that 80.1 per cent occur after forty (Table IV). What the number of cases of syphilis is in the United States and what per cent of these develop cardiovascular disease is very difficult to ascertain. I can find no adequate estimate of either group. In the Registration Area for 1920, the death rate for syphilis is placed at 9.1 per 100,000 population or 9,100 deaths. Stadler[57] puts the occurrence of syphilitic aortitis among syphilitic autopsies in the Leipzig Pathological Laboratory at 82 per cent. Hubert[58] gives the ratio of aortitis to visceral syphilis at 70 per cent. At this rate there would be 7,362 cases of syphilitic aortitis in the country, a rate of 7.36 per 100,000 population. In comparison with this figure, the incidence of syphilitic aortitis among general autopsies is very high. Gruber[59] (p. 96) gives the figure as 4 per cent (4,000 per 100,000 population), Lamb[60] as 4.58 per cent, Oberndorfer[61] as 6.89 per cent. In a revision of the Registrar General's Mortality Statistics by Osler,[62] apoplexy, aneurysm and aortitis, organic diseases of the heart, and diseases of the arteries, all told caused 92,564 deaths; of these 12,000, 12.9 per cent, were due to syphilis. In Bellevue Hospital[63] of all admissions in 1915, 30.5 per cent are said to be syphilitic. In certain industries in New York those infected are 22 per cent.[63] Elsewhere in the country the rate falls as low as 7 per cent.[63] Since the introduction of the Wassermann reaction, the number of cases in general medical clinics diagnosticated as syphilis has increased. In 1896 (Mengel,[64] Leipzig) it was said to be rare; in 1919 (Adlmühler,[65] Munich) it was put at 18 per cent and in 1924 (Wyckoff and Lingg,[31] New York) at 8.6 per cent. Steinfield, Pfahler and Klauder[66] found it only in 11 per cent of syphilitic males,

a low figure in a group which would generally be regarded as favorable for yielding a high figure.

The matter may be summed up in the following way:

Mortality		
Syphilitic deaths. Registration Area. U. S.		9.1 per 100,000
Syphilitic cardiac deaths are of all cardiovascular deaths		
	Registrar General's Report	12.9 %
Of syphilitic autopsies	Syphilitic heart disease represents	82.0 %
Of general autopsies	Syphilitic heart disease represents	4–6.85%
Morbidity		
Syphilis	General morbidity	7–30%
"	in general hospitals (Bellevue, N. Y. C.)	30%
"	in industries N. Y. C.	22%
"	elsewhere in the United States as low as	7%
"	in syphilitic cardiovascular cases equals	11%
General cardiovascular disease-syphilitic cardiovascular cases equal		8–18%

A low estimate places the number of persons in the country infected with syphilis at about 1,000,000. In choosing this per cent I am following the example of a Royal commission[32] (p. 39). If 11 per cent represents the proportion that develops cardiovascular diseases in a syphilis clinic the number may be placed very roughly at 110,000 cases. And if 8 per cent (Wyckoff and Lingg) is the proportion of syphilitic heart disease in a general clinic, the number of syphilitic cardiovascular cases would be 120,000, on the assumption that the total number of cases of heart disease in the country is between 1,000,000 and 2,000,000 cases. This agreement is fair but it is based on the roughest of estimates and is entitled to no great confidence.

But it is more important now to try to find the age incidence than the actual number of cases of syphilitic heart disease. (See Fig. 12.)

Stokes[32] has arranged 190 cases in the curve to the left in five year age groups. He has not published a scale, but by measurement I find that 10.9 per cent (24 cases) were below thirty-five years and 29.3 per cent (55 cases) under forty years. A large majority then is above forty. In the middle curve he shows that few cases relatively speaking have an incubation period less than ten years; that in most cases this period lasts from eleven to thirty years, the greatest number, sixteen to twenty years. If syphilis is acquired in the second and third decades and if the time before the development of symptoms is usually about twenty years, the appearance of these would generally be expected about age forty. Mackenzie (1908) mentions a case (quoted by Romberg[30]) in which cardiovascular phenomena were discovered seven weeks after infection; but it is unusual to find them before two years.

If now the distribution of heart disease according to etiology and age groups is undertaken it is found that a curve expressing the sum of the cases of syphilis and of arteriosclerosis added together which occur both in public and private practice falls far below the curve of morbidity which one should expect and which would run parallel with

the mortality curve for these age periods. This statement applies to data collected not only in this country but also abroad. Wyckoff and Lingg have studied this problem in some detail and from their study follows a consideration of value for interpreting the data which come from the clinics for public patients, and perhaps also, but to a less extent, in private patients. These are the curves to which I have already

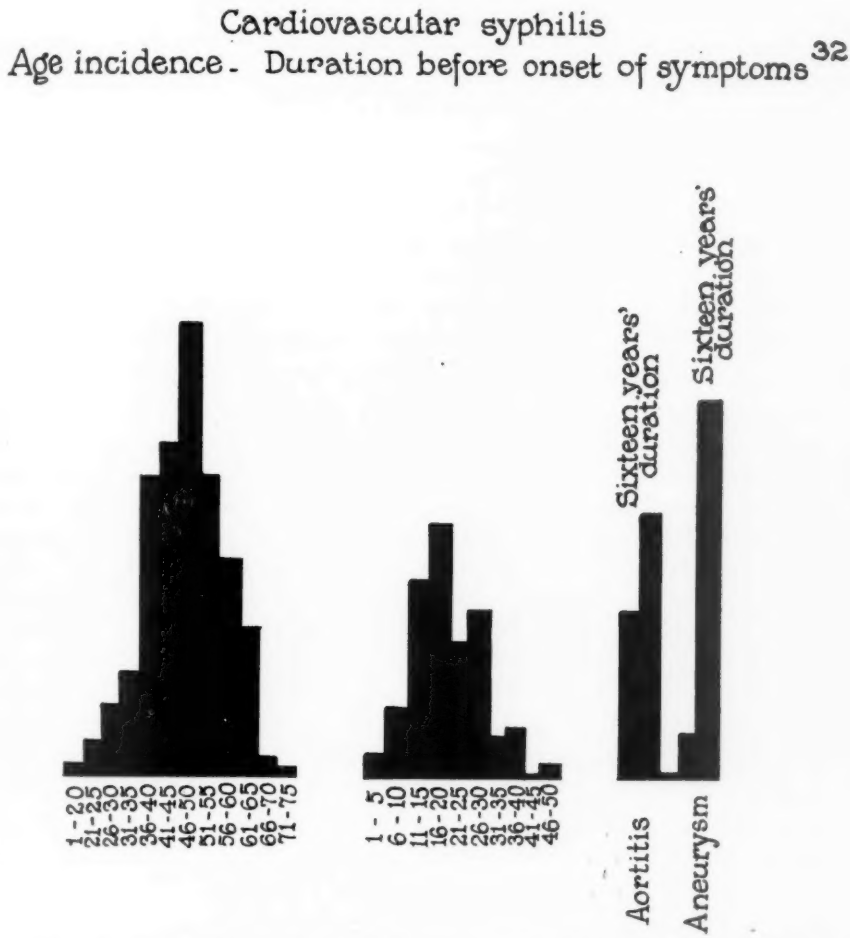


Fig. 12.—In the figure to the left, the relative incidence of cardiovascular syphilis for various age groups is given. In the middle figure is indicated the relative number of cases in which the duration between infection and onset of symptoms equalled the number of years given below. To the right, the division between the long and short columns in each case is sixteen years. Before sixteen years more cases of aortitis (and of aortic valvular insufficiency) are detected than of aneurysm. Aortic insufficiency has a shorter "incubation" period than aneurysm, apparent rather than real, because on account of its conspicuous physical signs it can be detected earlier than aneurysm. (From J. H. Stokes,[32])

referred. If it is true that the natural history of heart disease whether from rheumatism, from syphilis or from old age follows a usual course, then the curve of morbidity should follow the curve of mortality in

some usual fashion. The curve of mortality must, within limits of course, be considered as the norm.

In these curves (Fig. 13) taken from Wyckoff and Lingg the mortality for New York is given in the uppermost. Obviously the curves for ward patients and the curves for private patients do in some measure resemble the mortality curve, but the curve for public ambulatory patients and of course the curve of all ambulatory patients public and private together fails signally to resemble it. In the first place the apex of the second mode of the public ambulatory patient curve is found to be twenty years before the apex of the mortality curve and ten years before that of the private patient curve. The public patient curve moreover falls abruptly ten years earlier than that of the private patient curve. Wyckoff and Lingg think furthermore that the first part of this curve is higher than it should be because the numbers were augmented by the inclusion of patients brought to the Bellevue clinic from outside the Bellevue district, from the schools and from social service sources not connected with the hospital. There results in consequence a distortion of the curve which might occur elsewhere also. Why the second portion of this curve, that after age forty, fails to follow the mortality curve is not clear. Indeed the matter is difficult to understand, but Wyckoff and Lingg suggest the following explanation. People come to the clinics in early years because rheumatism is a dramatic disease and entails great suffering. The heart disease which results from it occurs when people are quite young and when the hope of a useful life is still strong. Accordingly they seek relief. The clinic curve is consequently high. Heart disease in the older age groups comes on insidiously. The meaning of the symptoms is misunderstood. The outlook in life is no longer full of promise. Economic pressure has been relieved either on account of savings or because patients are supported by children or otherwise. The situation is one which in any case is anticipated as part and parcel of the gradual process of decay. Patients do not come to the clinic; they do not seek advice; they accept the inevitable. The clinic curve falls, precisely at the moment when one would expect it to be high. If this description represents the situation in public practice the curve for private practice ought to differ from it and in point of fact it seems to do so although it does not follow the mortality curve as closely as it might. But the experience here is small and it is not beyond possibility that the argument which applies in public practice applies also in private. This is a subject which requires further and more detailed study. But in these considerations there is included a warning. Data obtained especially from public practice require scrutiny with the view to making certain that the samples offered as illustrative of the course of disease actually are so.

Organic heart disease
Curves of morbidity and mortality[31]

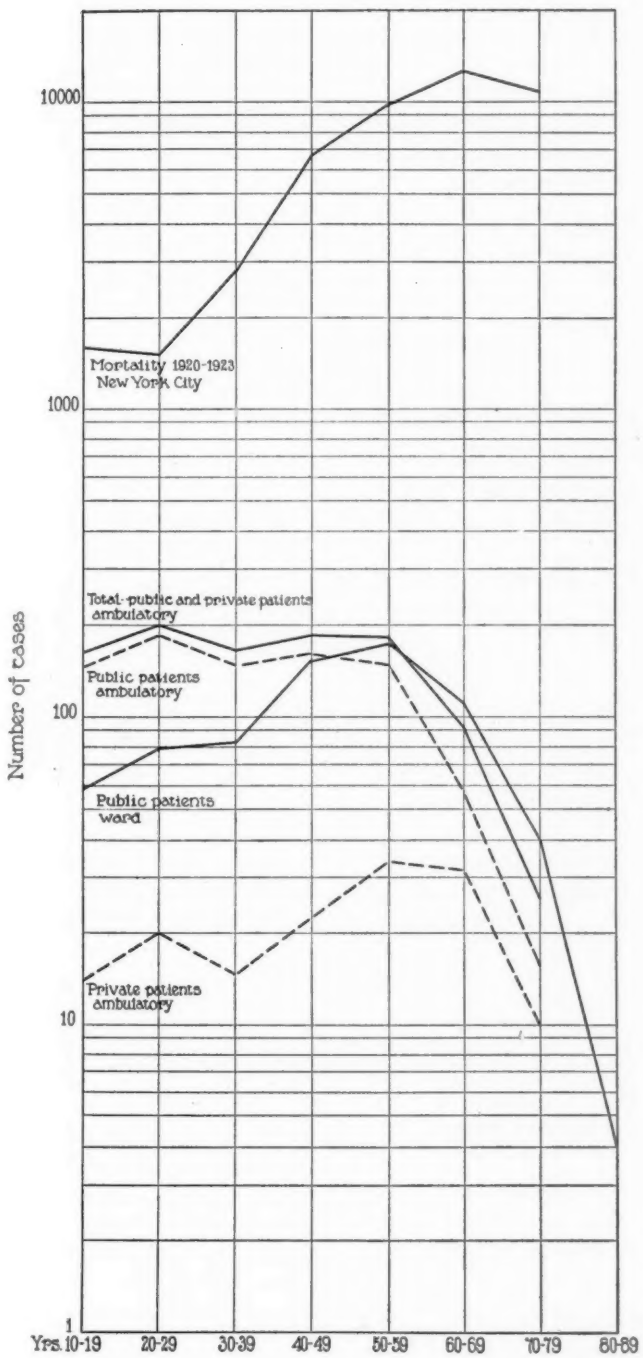


Fig. 13.

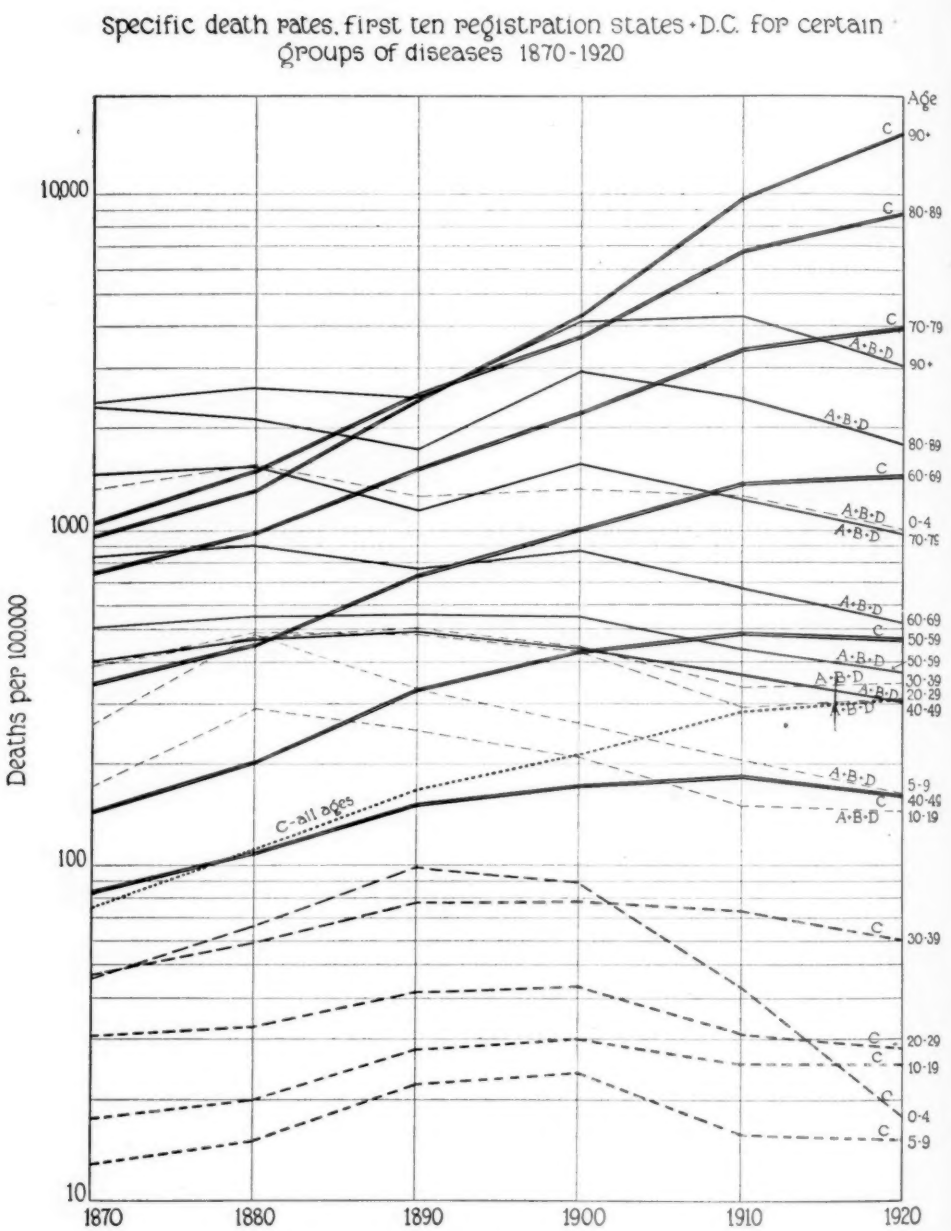


Fig. 14.

With the bearing of race and of sex on the incidence of heart disease I propose not to deal. Their influence on the phase of the problem I am discussing is not sufficiently clear. That girls at the age of puberty to twenty, according to Osler, or to thirty-four, according to the Practitioner's Enquiry,[9] fall subject to rheumatic fever twice as

often as boys, though contrary opinions are also expressed, and that heart disease due to syphilis is more common in men, is well known.

It appears also to be a fact that the duration of life in negroes subject to heart disease is a decade less than among the white population. The incidence of heart diseases among them seems to be greater everywhere in the Union, as is seen in the statistics of mortality when the State groups are studied; theirs exceeds the rate of the white population by 26 to 68 per 100,000 wherever their population is over 1,000,000. When it is small the rate rises as it must if the scale is per 100,000. The difference is assigned by Dublin[12] to the greater incidence of syphilis, malaria and typhoid fever. Higher rates in earlier age groups may naturally be due also to decrease in natural longevity.

I have laid so much stress on age forty as a dividing point not only because, as it appears, the majority of cases before this period have their origin in infectious diseases and especially in the rheumatic group, but because I wish to emphasize the fact that these are relatively speaking a small number, namely one-sixth, of the total; that in point of fact by far the greater number of deaths due to heart disease, namely, five-sixths, occur after this period. On the far side of age forty, a certain number are the sequels of syphilis. But presumably the larger number results from what is usually called degenerative disease; from arteriosclerosis. I wish to contend that these conditions are properly not diseases at all, but that they represent differentiation phenomena in the course of the ordinary growth process. Multicellular animals, and the argument need be suggested only, have if not a fixed, at least an anticipated longevity. From the point of view of expectancy years have been added to life. Unfortunately this fact has sometimes been interpreted as being a biological rather than an arithmetical phenomenon. There is sometimes confusion between the meaning of expectancy and of longevity. The duration of life has not been extended; on the contrary the attainment of its natural length has merely been rendered possible. How this may have come about at least in part has appeared in studying the relation between the declining death rate from infectious diseases and the rising one in chronic diseases (Figs. 3 and 4). But the conclusion that the increased number of deaths from heart disease has occurred in the older age groups exclusively results from the study of specific death rate curves. (Fig. 14.)*

All the heavy dotted curves marked *C* at the bottom of the figure that is to say curves of heart disease, one for each decade *below* age forty run, to all intents and purposes, a horizontal course. The curve for ages 0-4 on the contrary has fallen sharply. Into the cause for this I need not enter. All the light dotted curves in the midregion of

*I am indebted to Miss Alice Whittemore for the data in this and the next two curves.

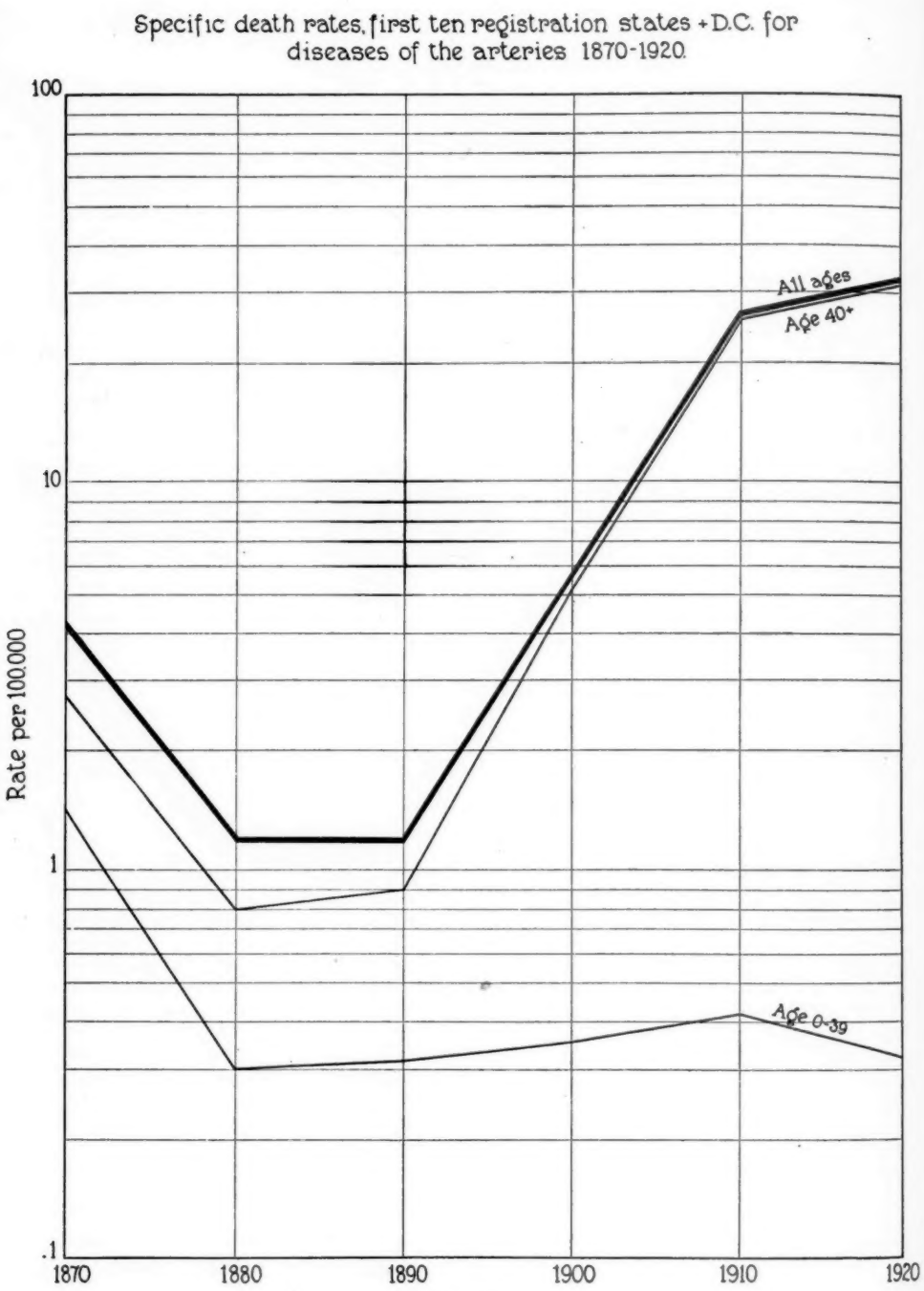

Specific death rates, first ten registration states + D.C. for diseases of the arteries 1870-1920
100
10
1
.1
Rate per 100,000
All ages
Age 40+
Age 0-39
1870
1880
1890
1900
1910
1920

Fig. 15.

the figure, one for each decade marked *A B D*, that is to say the curves representing infectious diseases *below* age forty, have likewise fallen. All the light solid lines marked *A B D* one for each decade over age forty have either fallen or remained horizontal, except for age ninety and this one too has fallen in the last ten years. That the death rate from heart disease below age forty has fallen is apparent also in Curve C_2, Figs. 3 and 4. In what decades the rates from infectious diseases have been affected, the movement of the total rate of which is seen in Figs. 3 and 4, is shown in Fig. 15 in which age specific curves are exhibited. It appears on analysis then that the rise in the death rate from heart disease has occurred exclusively after age forty, as the double lined curves one for each decade marked *C* show, and the rise has been the higher the higher the age.

If the increase in deaths from heart disease has resulted from transferring deaths due to defects in the arterial system or from some other indefinite heading to the cardiac group, a fall in the curve for diseases of the arteries should have taken place. That this is not the case is seen in these curves. (Fig. 15.) And that the changes have taken place exclusively above age forty is apparent from this further set. (Fig. 16.)

A summary of the changes which have taken place in the past ten years is exhibited by the curves of Fig. 17.

In that to the left are age specific curves for 1910 and 1920, both for males and females.* With the exception of a single half decade there is a fall in rate for each decade before age sixty. The fall between ages forty to sixty concerns the year 1910 only; in earlier years there is a conspicuous rise as has already been shown. Above age sixty there is a uniform elevation of the 1920 curves above those of 1910.

In the figure to the right there is still another expression of the same phenomenon. Under age sixty, the rate fell 0.09, above age sixty, it rose 17.12.

Aside from the matter of treatment with drugs and by other means, of which I have already spoken in connection with rheumatic fever and syphilis, the large number of persons who suffer from chronic heart disease places a charge on the public to see to it that provision in appropriate institutions is made for their care. Public provision at least of two sorts is requisite; the hospital for what may be called the more acute or urgent phases of these diseases or, in the case of rheumatic fever, during the period of active infection in the febrile stage; and in the case of already established chronic disease, in the period when heart failure first appears. Later, for both types of case, further provision is desirable when the course of disease is less stormy and while reconstitution on a new level of activity is being accomplished

*For the data for these curves I am indebted to Dr. William H. Davis, Chief Statistician for Vital Statistics, Department of Commerce, Bureau of Census, Washington.

Specific death rates, first ten registration states plus D.C. for diseases of the arteries 1870-1920.

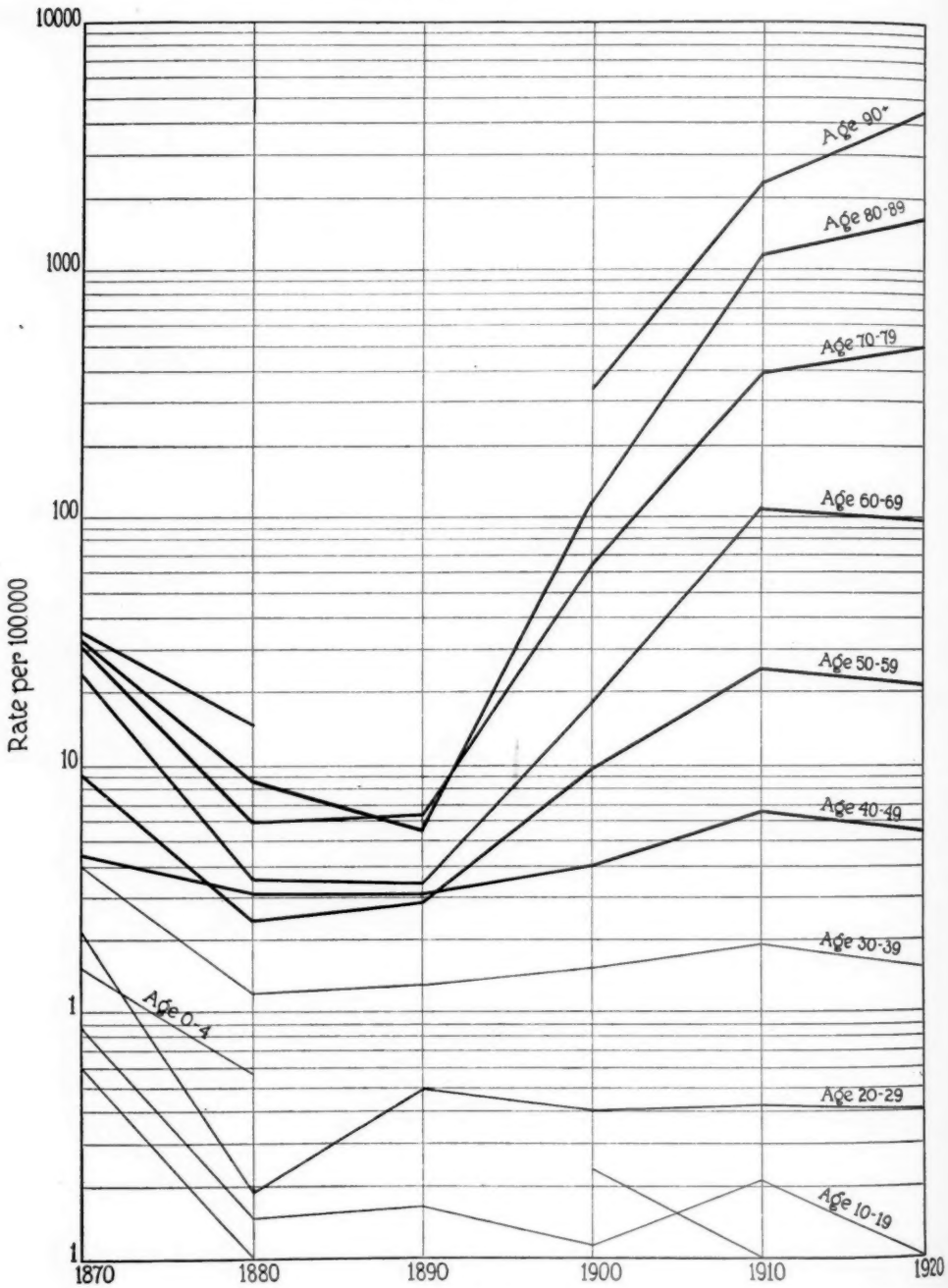
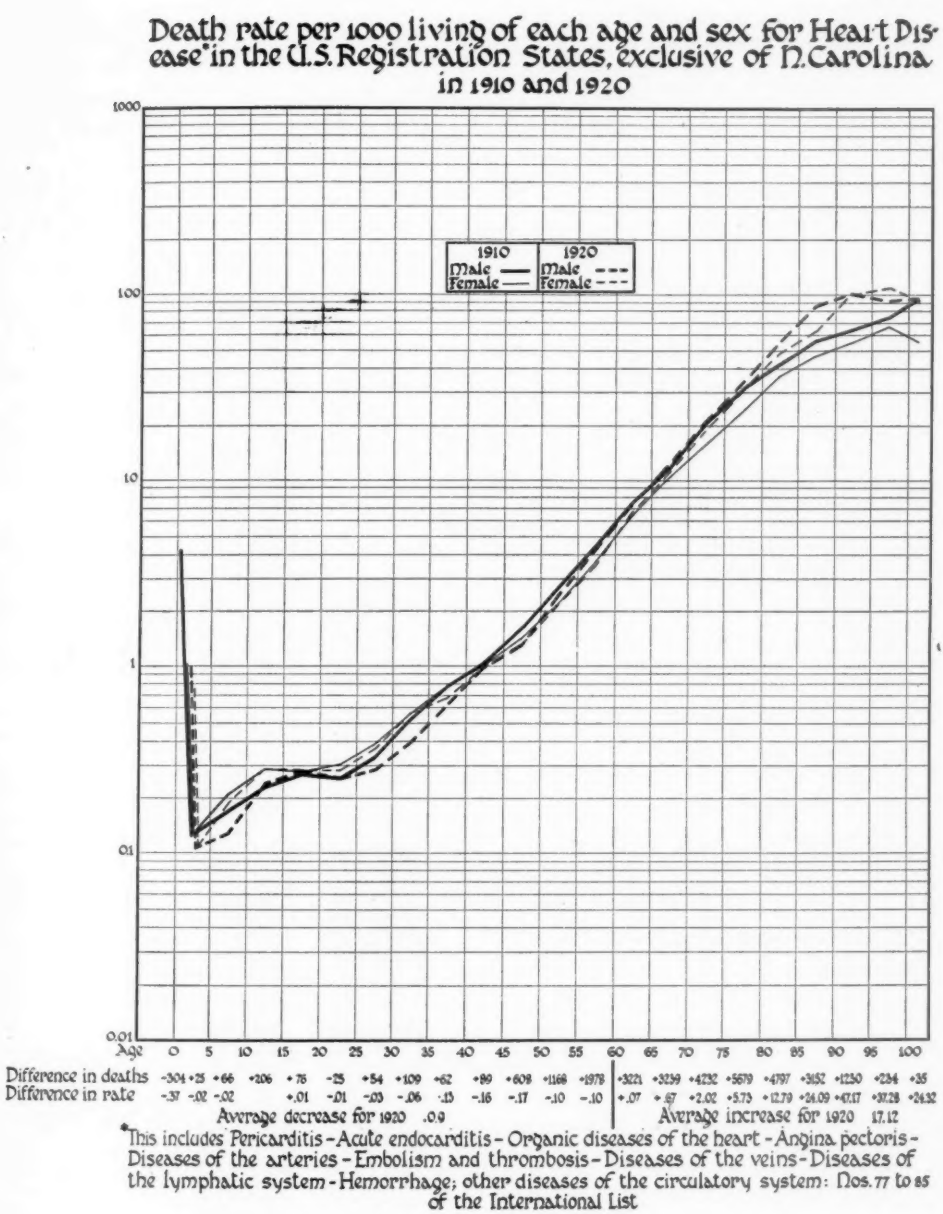


Fig. 16.



*This includes Pericarditis - Acute endocarditis - Organic diseases of the heart - Angina pectoris - Diseases of the arteries - Embolism and thrombosis - Diseases of the veins - Diseases of the lymphatic system - Hemorrhage; other diseases of the circulatory system: Nos. 77 to 85 of the International List

Fig. 17-A.

and a new way of life learned. What has come to be known as the convalescent home now supplies the second need.

Unfortunately I do not possess data covering the hospitals in the whole country. But in New York, I have figures which Emerson[67] has published. He found in 1920 or 1921, that in ten of the larger New York hospitals 98,838 patients were admitted. Of these 4.6 per cent

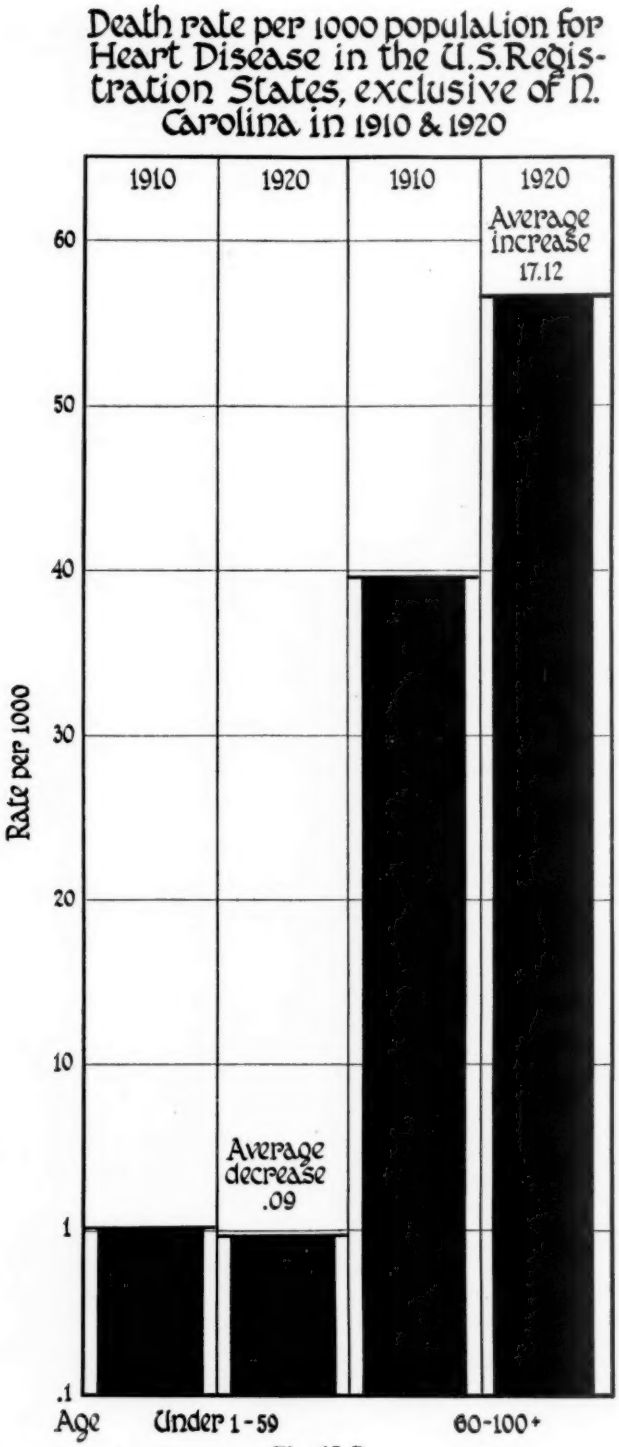

Death rate per 1000 population for Heart Disease in the U.S. Registration States, exclusive of N. Carolina in 1910 & 1920
1910
1920
1910
1920
Average increase 17.12
60
50
40
30
20
10
1
.1
Rate per 1000
Average decrease .09
Age
Under 1 - 59
60-100+

Fig. 17-*B*.

(4,522 cases) were cardiac. The average stay in hospital for each cardiac patient was fifty-two and two-tenths days. The per cent of all hospital days care given to cardiac patients was 9.35. Notice that cardiac admissions were 4.6 per cent, whereas cardiac patients took 9.35 per cent of the hospitals' attention. The cost of a cardiac patient in the general hospitalization studies averaged $257.27. He suggested that a one hundred-bed convalescent cardiac hospital was needed. Dr. Emerson has in a letter explained to me the course of his reasoning. On account of its interest, I repeat his argument. Although heart patients represent only 4.58 per cent of all general hospital patients, they require, or at all events receive, twice as much care in proportion to their numbers, as other patients do, or 9.35 per cent of the total number of days given in the hospital study. Assuming that they were still in need of further bed care, probably an additional twenty to forty days per patient, a total stay of forty to eighty days of hospitalization for each cardiac patient is estimated. Those of us who have had experience in hospitals know that not even this allowance suffices. They can in point of fact be better and more economically cared for elsewhere, as in convalescent homes. To find a basis for calculating the size of the home needed, Dr. Emerson proceeded as follows: The ten New York hospitals discharged 565 heart patients in one year. Assuming that they were still in need of care say for additional twenty to forty days per patient, a total stay of forty to eighty days is obtained. A one hundred-bed hospital performing this service for 565 patients, the number of heart patients discharged in a year, could provide an average of 64.5 days per patient. Dr. Emerson goes on to say, "Of course the correct way of determining the extent of the need for beds for chronic heart patients would be by studying the disposition of these patients on discharge from general hospitals and inquiring into the adequacy of home or other care provided."

There are meanwhile about New York, 312 beds the year 'round available for heart patients in institutions, the total capacity of which is 910 beds; that is to say 34.2 per cent of the beds in eleven convalescent homes.

In the country at large, the convalescent home has likewise been developed. Whether the number of beds which they offer suffice for the local requirements I do not know. There are 174 homes in 22 states, with a capacity of 10,201, about 60 per cent (6,076) being available all year, the remainder (4,125) for the summer only. They provide for cases of maternity, orthopedic defects, tuberculosis, a few only exclusively for cases of heart diseases.

Meanwhile, with the decline in the death rate and in morbidity from tuberculosis, the expectation should be realized, that of the large numbers of beds provided for tuberculosis, a certain fraction would be relinquished for heart disease. G. J. Drolet[69] the statistician of the New

TABLE VIII

SUMMARY OF NATIONAL DIRECTORY OF CONVALESCENT HOMES[68]

STATES	HOMES	YEAR-ROUND BEDS	SUMMER ONLY	TOTAL
Alabama	2	12	20	82
California	11	489	100	589
Connecticut	5	120	280	400
Georgia	1		50	50
Illinois	8	292		292
Kentucky	2		80	80
Louisiana	2	30	50	80
Massachusetts	24	476	228	704
Maryland	4	78	44	122
Michigan	1	135		135
Minnesota	3	187		187
Missouri	4	72	50	122
New Hampshire	1		10	10
New Jersey	23	875	668	1543
New York	55	2574	2210	4784
Ohio	4	160	40	200
Pennsylvania	18	479	75	554
Rhode Island	2	45	180	225
South Carolina	1			
Texas	1	24		24
Virginia	1	28		28
Washington, D. C.	1		40	40
22 States	174	6076	4125	10201

York Tuberculosis Association, in compiling the resources of the country concludes that this is not the case, but that on the contrary, the country is in arrears, 25,864 beds. He bases his computation on the fact that there were 99,579 deaths from tuberculosis (1924) and only 73,715 beds. Presumably the deficit he cites, leaves out of account those cases which find care at home, those which are provided for in institutions for the insane (5,500) and those for prisoners in state institutions (1,300). It might be pointed out that the figures Drolet cites are based on the rate of one institutional bed for each patient; but he has pointed out the fact that this is an arbitrary arrangement especially in view of the fact that "by actual count only 20 per cent of the deaths from tuberculosis in the United States take place in institutions." Nevertheless it has been found that the beds can be kept continuously filled. In 1925, patients in tuberculosis hospitals were found to stay on an average, close to six months, namely, one hundred and seventy-four days.[69] But in general it appears that beds for heart disease cannot be acquired from beds fallen vacant from use for tuberculosis, even provided that hygienically, this could be accomplished. There are states, however, in which beds for tuberculosis are in excess of the apparent needs, as for instance in Arizona, Colorado, Connecticut, Massachusetts, and New York. In other states there is, however, a deficit, as for instance in Maryland, California, Ohio, and Pennsylvania. What arrangements it is possible to make in the interest of

the transfer that has been suggested it might be important to investigate.

I trust enough has been said to show that, from practically every point of view, information is inadequate, so far unavoidably inadequate. Geographical distribution, etiology, age relation, infectivity, heritability, therapeutics—wherever the subject is touched there is uncertainty. Because of the general chaos in which the whole matter of heart disease lies and because of the general lack of widespread information, there has been formed the association to which I have already referred. In New York, where the pioneering has taken place, alongside of the heart association, there arose cardiac clinics which also formed an association. There are now upwards of fifty of these clinics well distributed through the greater city. Next, the association and the clinics united and finally all were absorbed by the New York Tuberculosis and Health Association. Parallel with the New York City movement, a national association has been formed. The Heart Committee, as that part of the New York Tuberculosis Association is called which deals with heart disease, has as one of its committees a Committee on Research. This Committee has labored for several years with methods for collecting accurate and adequate data on the more general aspects of these diseases. It struggled for several years with devising forms[70] of reporting and believes that the method which was developed is adequate to its purpose. The forms which were produced are used in the Bellevue Heart Clinic, the largest one in New York, and have served as the basis of a number of the statements I have been able to make in this report. If you were to look through the publications dealing with certain aspects of this subject, you would I think be surprised to learn how much information has flowed from this single source. If it is possible to study cases in this manner at the Bellevue Clinic, it is, as we know already, possible elsewhere. Even with slender resources, this investigation has gone forward, with a very small permanent staff. With a grant recently acquired from the Commonwealth Fund, this study after its period of trial is to be expanded so as to include more clinics and to be more broadly based. Great effort has been made to safeguard at the source the value of the data. Agreement has been attained on nomenclature and classification, definition, and diagnosis. Trained secretaries see to it that duplicate records from the various clinics are not brought together for collation until the record of each case has been edited and revised. The original records are the property of the clinics and are retained by them for whatever use the clinics desire. Were the data entered for which there is provision on the record forms, each phase of the whole problem which I have been discussing could receive adequate exposition, instead of the fragmentary information I have been able to lay before you. Accuracy of information can be attained only by

this or by some other similar method. But the pursuit of the aim will lay considerable obligation on the public-mindedness of those physicians who participate in this enterprise.

In the course of this exposition, I referred to the curves of Wyckoff and Lingg in considering which there developed a danger encountered in drawing the morbidity curve, first on account of dilution among the younger and second on account of paucity of cases among the older age groups. These are difficulties which can be avoided; there should be sought methods of compensating the defect, especially in the older age group. A utilization of the records in private practice can perhaps supply this need. That this method is practicable has already been demonstrated in New York, and that this example be imitated is distinctly desirable.

It has been the purpose of this report to place emphasis on the meaning for the public health of certain aspects of the heart diseases and of their occurrence. The most desirable plan for drawing attention to matters of this nature utilizes the statistical method; and this would also be the best method in a perfect world. Under the circumstances the use of the method has revealed how imperfect a world this is for just this purpose. But however imperfect the method, no other one is designed to present the facts. To eschew the method because the results are defective and to fly to an extreme in which the classification of cases is neglected but in which individual ones are described meticulously instead, begs rather than meets an important issue. Individual cases adequately and completely described remain without meaning from the point of view of probability until they are assembled in groups. But statements like this are elementary and would scarcely require mention were it not for the fact that, especially among the best observers, the fact escapes notice that data as data remain sterile; not until they are brought into action in a larger world of relevance do they take on significance. That accumulations of facts such as I have assembled leave much to be desired is not surprising; it is on the contrary encouraging to reflect that a sound beginning has been made and that ways are being devised for improving the methods of acquiring and of tabulating knowledge of this sort.

SUMMARY

It is important to review certain results which issue from this inquiry.

1. Attention should perhaps first be drawn to the fact that unlike tuberculosis, heart disease concerns an organ and not a simple etiological moment. Diseases of the heart result from a number of different injuries. In the case of the heart, three main groups can be distinguished: first, that associated with rheumatic fever; second, syph-

ilis; and third, arteriosclerosis or as I prefer to call it the senescent process.

2. There can no longer be doubt of the fact that rheumatic fever affects persons in the first three decades predominantly; that syphilitic heart disease is rare before the third decade and is often delayed two decades more; and that if due allowance is made for the age of occurrence and for the duration of these two disease types, the preponderant number of deaths occurs after age forty.

3. It is borne out by study of the curves which relate infectious and heart diseases, that the two have moved in opposite directions. The curve which represents the former has been falling, while that of the latter has risen. But the relation is not quite simple, for neither curve travels a smooth course. It is, however, possible to notice that at certain points, changes in the direction of both curves have taken place. It is furthermore noticeable that there occurred a delay in the increased rise of the curve from heart disease for a number of years after that of the infectious diseases began to fall. That this period is seventeen years may have a meaning but it is not an obvious one and no insistance is placed upon it. That there should be a delay like this is easily comprehended; if individuals fail to die of infection, they will die in some other manner, and of affections which develop or are incident to life at later ages.

4. That the data which have been accumulated support this view seems clear, for the curves all show that the increased rate of death from the heart diseases involves persons over age forty. Under this age, the rates, as these curves show have actually fallen. Additional confirmation of this view resides in the fact that the rate increases with each decade.

5. The inference to be drawn from these statements has an important bearing on the fears which have arisen on account of the obvious increase in the death rates due to the heart diseases. If as the data show, the increase involves the older age groups only, the result is altogether gratifying. If men are, as the old adage has it, as old as their arteries, it becomes an important consideration to learn how long these may live. If they live their full span of years, death from old age and death from circulatory defect may prove to be the same thing. To die so would turn out to be the method of choice for the human organism; at all events, to realize it appears to be the direction which the course of events I have been describing seems to be taking.

6. Environment, climate, latitude all appear to influence the incidence and course of rheumatic heart disease. But the data inspire no great confidence and suggest that the conditions under which they are collected be more precisely defined.

7. Experiences on the subject of treatment have been described. Apparently, from a remedial point of view, it is only in the rheumatic variety of heart disease that success can be anticipated from the use of methods designed to close the avenues of infection. The suggestion that patients be treated, as are the tuberculous, with continuous prolonged rest, deserves consideration. Too little is known now to justify the adoption of an opinion on this point.

CONCLUSION

It was my intention to show in this very incomplete summary that from the point of view of the public health, the problem of heart disease is not simple as was that of tuberculosis, but manifold. It includes disability from infectious diseases such as rheumatic fever and syphilis, and disability incident to the process of aging. The effort to relieve rheumatic fever by removing areas of infection still wants prosecuting before a judgment on its value can be given. To prevent the onset of the disease is still impossible. Theoretically the situation in syphilis is more fortunate; practically the methods of prevention and treatment offer enormous difficulty. Nor has a final conclusion been reached on the value of treatment. There also more knowledge is wanted. The disabilities dependent solely on age, the major aspect of the problem, must elude approach on the side of etiology; to provide relief from distress must be the direction in which to expend effort.

If the infectious aspect of heart disease is relatively speaking small, smaller than is often thought, that is a happy discovery. But that the rate of so-called chronic heart disease is high and is constantly mounting, that is a condition in which those may take satisfaction who believe increased length of life for more persons is one of the great blessings of men. The rise may be alarming but it is not malign.

So many matters are, as I have tried to indicate, not clear, that there must be general agreement that the idea which underlies the effort to accumulate information is sound and its prosecution desirable.

I should like to conclude these remarks with an expression of the pleasure I felt at receiving your invitation to make them as well as of the honor I know it to be, to be included among those who have had the opportunity to deliver De Lamar Lectures.

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THE RADIOGRAPHIC SIGNS OF PULMONIC INSUFFICIENCY*

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IN 1889 Graham Steell[1] described for the first time the murmur which bears his name and is attributed to relative pulmonic insufficiency secondary to increased intrapulmonic pressure. His views have been confirmed since then by the experiments of Gibson[2] and by the post-mortem findings of Pawinsky,[3] Pitt,[4] Hall,[5] Sailer,[6] Goodman[7] and others. The murmur occurs chiefly in mitral stenosis[8] and very rarely in cases of kyphoscoliosis[9]; of thoracic aneurysm[10, 11, 12]; of embolism,[13] sclerosis,[14] stenosis or thrombosis of the pulmonary artery,[15] and in fulminating endocarditis.[16, 17] It has also been heard in chronic lesions of the lungs[18] and in malformations of the pulmonary valves.[19, 20]

The diagnosis of pulmonic insufficiency is based on the presence of a soft blowing diastolic murmur, heard best in the second or third intercostal spaces to the left of the sternum in the absence of any signs of aortic disease. Occasionally the murmur may be transmitted as far down as the xiphoid region and upwards to the left towards the acromioclavicular joint. Ortner[21] still believes this to be the diastolic murmur of mitral stenosis. The differential diagnosis, however, is from that of congenital heart disease, such as pulmonic stenosis and patent ductus arteriosus, and more so from cases of mitral stenosis that might present an aortic insufficiency without conclusive accompanying peripheral signs such as a low diastolic blood pressure, water-hammer pulse, capillary pulsations and a pistol-shot femoral sound.

From a study of three cases, I have found a radiographic sign which seems to be of real value in the differential diagnosis and this I wish to discuss.

The x-ray (6 foot) plate of a normal heart presents on its left border from above downwards, the aortic knob, the pulmonary artery, the left auricular appendix and the left ventricle.

In uncomplicated cases of mitral stenosis, with enlargement of the left auricle, as well as the right ventricle and the pulmonic conus, there is a tendency for the heart to rotate to the left as well as back-

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wards and upwards. The left border then, in the usual cases, presents from above downwards, a very small aortic knob, a slightly dilated pulmonary artery, a prominent left auricular salient (pulmonic conus plus the left auricular appendix) and the enlarged left ventricle, especially when mitral insufficiency has been present for some time. The predominating bulge in these cases is usually immediately above the left ventricle, supposedly involving the lower portion of the left auricular salient. Cases of severe mitral stenosis show, as a rule, an increase in the left auricular salient as a characteristic feature of this condition. The pulmonary artery, except in children with mitral stenosis, is slightly dilated.

In cases complicated by pulmonic insufficiency, however, the pulmonary artery is widely dilated and shows so in the radiographic film.

Fluoroscopically, cases with mitral stenosis when placed in the right anterior oblique position, show as a characteristic sign of the disease, a marked encroachment of the left auricle upon the retrocardiac space. This is true also in cases where there has been an accompanying mitral insufficiency of long duration so as to cause left ventricular hypertrophy. With the patient in the same position, there is only moderate bulging of the pulmonary artery visible in the uppermost part of the cardiac shadow towards the anterior part of the chest. In the cases of mitral stenosis, however, which present a diastolic murmur at the second or third intercostal spaces to the left of the sternum (in the absence of signs of aortic disease), the pulmonary artery almost assumes the first upper curve of the left side of the heart in the form of a huge bulge which shows just as prominently in the right anterior oblique position. The artery does not pulsate forcibly as in congenital lesions of the heart. When the left ventricle is not markedly enlarged this pulmonic bulge may also be seen in the uppermost space adjacent to the spinal column with the patient in the left posterior oblique position.

I have never observed a similar dilatation of the pulmonary artery in cases of mitral stenosis accompanied by aortic insufficiency.

The radiograms of cases with mitral stenosis accompanied by pulmonic insufficiency, simulate very closely those of congenital lesions of the heart, such as a patent ductus arteriosus, pulmonic stenosis and ventricular septal defects. As a matter of fact, Dietlen described this type of picture as that of a mitral lesion combined with congenital heart disease.

The electrocardiographic tracings of almost all congenital lesions showing bulging of the pulmonary artery, present as a characteristic sign, besides increased voltage and the right ventricular predominance, a T-wave of very large size (about 5 mm. high). This I have observed in the last ten consecutive cases recorded at our cardiographic laboratory. While right ventricular predominance is a com-

mon finding in cases of mitral stenosis with marked dilatation of the pulmonic artery, the voltage is usually lower than in the congenital lesions, and the T-wave is not as prominent. Where aortic insufficiency is present with a combined mitral lesion, the usual electrocardiographic findings are those of left ventricular predominance instead of right.

The following cases illustrate these points:

CASE 1.—No. 8706. The patient, a boy, aged sixteen years, presented himself to the hospital with a history of having heart trouble for about seven years. He had been well up to that time when a physician advised him to go to bed because of a slight rise in temperature. After a few weeks of general malaise, he became well and was up and about, going to school until three years ago. At that time he was compelled to stay in bed for several months because of persistent fever. Two years prior to admission for the first time his joints became swollen, red and painful. On admission, he had a productive cough, was short of breath and felt very weak.

Physical examination revealed a poorly developed and poorly nourished young adult male who appeared chronically ill and very dyspneic. He was slightly pigeon-breasted. The precordium was heaving. The apex was in the fifth intercostal space in the anterior axillary line. Palpation revealed a long presystolic thrill over the precordium in the region of the fourth and fifth intercostal space. Over this region the heart percussed enlarged to the left of the sternum. A rumbling presystolic and a prolonged diastolic murmur were heard at the apex. The first sound was markedly accentuated. A soft diastolic murmur different in character from that at the apex was heard at the second intercostal space to the left of the sternum. The murmur was heard equally well with the patient in any position and was accentuated during inspiration. The pulses were equal and regular, the blood pressure was 110/50 mm.

The lungs were resonant throughout, except for a few moist râles at both bases. The abdomen was slightly distended. The liver edge was palpable three cm. below the costal margin in the midclavicular line. The blood Wassermann reaction was negative.

The x-ray of the heart (6 foot plate) showed it to be enlarged to the right and to the left and downwards (measurements were not given) with very marked prominence of the pulmonic artery.

The patient died from cardiac failure and the autopsy performed by Dr. Seecof two hours later showed the following: (Only the heart is reported here.)

"The heart was slightly enlarged. The pericardial surfaces were thin all over, smooth and glistening. On section there was moderate hypertrophy and dilatation of the right auricle. The tricuspid ring which was felt as a dense fibrous band measured 11 cm. There were numerous pin-head-sized translucent vegetations on the auricular surfaces of the tricuspid valve along the free borders of the leaflets. In places, the vegetations were confluent and covered over by endocardium evidently healed. The right ventricle was moderately dilated and its musculature slightly hypertrophied. The striking feature was the marked hypertrophy and moderate dilatation of the pulmonary conus. The right ventricular wall near the apex measured 4 mm. At the conus, it measured 7½ cm. The pulmonary leaflets were normal except for numerous, minute pin-head vegetations along the free borders. The left auricle was moderately thickened, but not dilated. The endocardium was markedly thickened.

"The mitral valve was represented by a funnel-shaped, thickened, fibrous structure with an opening about 1 cm. in diameter. There were numerous verrucose vegetations on the free borders of the opening. The left ventricle was slightly dilated and hypertrophied, measuring 15 mm. in thickness. The aortic ring, smaller than

the pulmonic, measured 6 cm. There was moderate fibrous thickening along the free borders, most marked at the corpora arantii. There were likewise a few pin-head recent vegetations on all three leaflets. The aorta showed no abnormalities and was strikingly free from any atheromatous involvement. The coronary arteries presented no abnormalities. The pulmonary artery, on the other hand, was widened, its walls thicker than that of the aorta, its intima was roughened and there was a small atheromatous plaque about 2 inches from the valve.''

Attention should be called here to the fact that it is unlikely that the pin-head vegetations on the pulmonic valve were responsible for the insufficiency. We have never seen any such dilatation of the pulmonic artery in the course of the verrucose endocarditis. Luttembacher's description of his cases has brought out this point very clearly.

CASE 2.—No. 52586. A female, aged twenty-six years was admitted to the medical service on January 23, 1926. Her chief complaints were shortness of breath and palpitations of the heart of three years' duration.

She had measles in childhood and scarlet fever at the age of ten. She has had frequent attacks of tonsillitis.

In 1921, about three months after her marriage, the patient was compelled to take to bed with a well marked attack of chorea. Because of the severe symptoms, a therapeutic abortion was performed with complete relief of her choreiform signs. About one year later, in 1922, she had a miscarriage at two months. Since that time she has been in bed a good deal because of weakness, shortness of breath, and palpitation of the heart.

Physical examination revealed a dyspneic, adult female rather poorly nourished and pale. The veins of the neck were distended. There was a heaving impulse over the precordium. The apex was in the fifth intercostal space, 12 cm. from the midsternal line. Palpation revealed a presystolic thrill over this region and a marked diastolic shock over the second intercostal space to the left of the sternum. Over the latter region the heart border percussed 6 cm. from the midsternal line. The first sound at the apex was loud. There was a presystolic thrill followed by a diastolic murmur. With the patient in a sitting posture, a loud blowing diastolic murmur was noted in the second intercostal space to the left of the sternum. The pulses were equal and regular. The rate was 88. The blood pressure was 98/62.

The lungs showed congestion at both bases and the liver edge was felt 2 cm. below the costal margin. The blood Wassermann reaction was negative.

Fluoroscopic examination showed a marked dilatation without forcible pulsation of the pulmonary artery in the ventrodorsal position. This dilatation was accentuated in the first position (right anterior oblique at 50 degrees). In the third position at 45 degrees (left posterior oblique) the pulmonary artery appeared enormously dilated and its encroachment upon the retrocardiac space was distinct from that of the left auricle below it.

Roentgen examination of the chest showed in both lower lobes a marked increase in the density. The shadows were due to a chronic pulmonary congestion with fibrosis. The heart was moderately enlarged to the left, most marked in the region of the pulmonary artery which showed a distinct bulge. Cardiac dimensions were M. R. 4.9 cm.; M. L. 8.5 cm. (Fig. 1.)

The electrocardiogram showed right ventricular predominence, the P-wave was very large and notched, especially in the second lead. The T-wave was negative in the third lead. (Fig. 2.) (Patient was not receiving digitalis.)

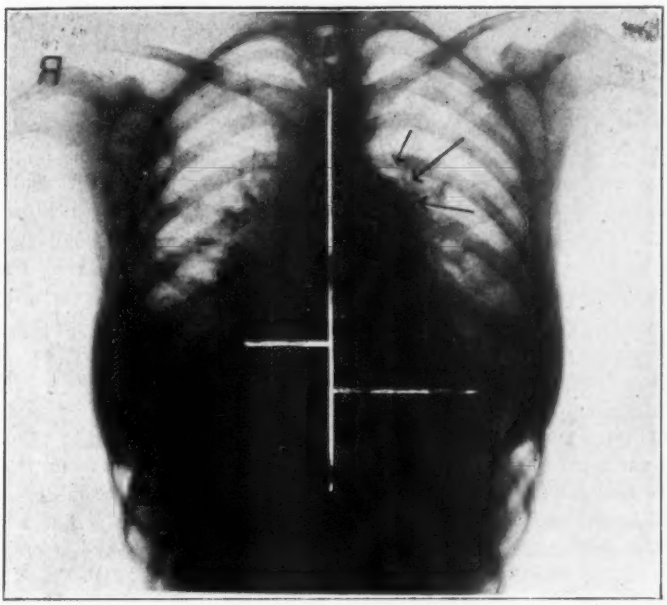

Fig. 1.—(Case 52586.) The heart is moderately enlarged to the right and to the left. M. R. 4.9 cm.; M. L. 8.5 cm. Note the marked bulging of the pulmonary artery.

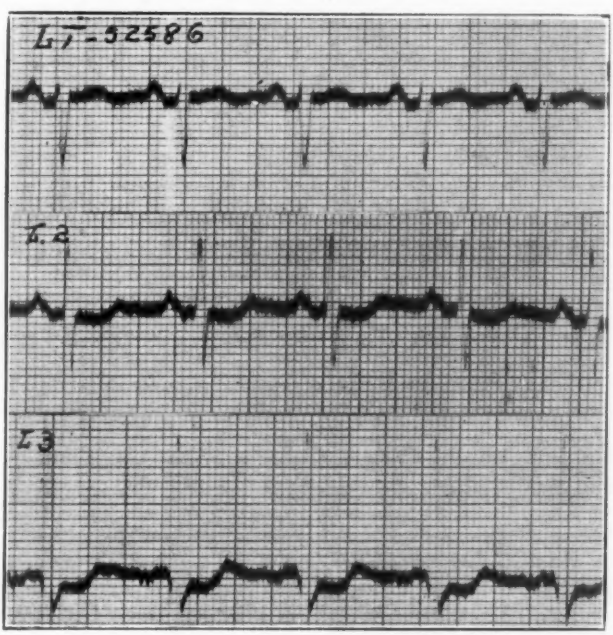

Fig. 2.—ECG. shows right ventricular predominance. The P-wave is large and notched, especially in the second lead. T-wave negative in Lead III.

The patient died from cardiac failure and the postmortem examination performed by Dr. Seecof a few hours after death showed the following: (The incision was limited to the vaginal route. Only the heart is reported here.)

"There were no adhesions or fluid in the pericardial sac. A few flattened hyalinized nodules were noted on the inner surface. The heart was slightly enlarged and weighed 320 gm.

"On inspection there was a striking disproportion between the right and left ventricular cavities. The right ventricle was the larger and occupied the entire anterior aspect of the heart. The left ventricle was very small and occupied only the extreme left lower border. The left auricle was almost completely hidden by the widely dilated pulmonary artery and conus. The right auricle which was markedly dilated formed the right border of the heart. Its epicardial surface was covered by a thick layer of organized fibrin. [The left margin of the heart, therefore, as seen from the front was formed by the pulmonary artery above, and the right border of the left ventricle below. The widely dilated pulmonary artery together with the conus obscured the left auricular appendix. This can be explained mainly by the increased rotation of the heart to the left, which takes place with the enlargement of the right cavities. It also interprets in this case the absence in the radiograph of the bulge on the left border immediately above the left ventricle, since the left auricle has been forced completely posteriorly by this change. That is why the left auricle could be seen in this position only when the patient was placed in the right anterior oblique. The curve immediately below the pulmonic artery is the upper part of the left auricular salient, namely, the pulmonic conus.]

"The tricuspid orifice admitted three fingers and measured 11 cm. across. The leaflets were slightly, though definitely thickened, the free borders slightly rolled. There were numerous small, flattened, translucent (not injected) vegetations along the line of closure of all three valves. The chordae tendinae were slightly thickened and the papillary muscles somewhat hypertrophied. The right ventricle was widely dilated and firm. There was a large milk patch on its anterior surface. The wall which was uniformly hypertrophied measured 10 mm. The endocardium was normal. There was moderate dilatation and hypertrophy of the conus of the pulmonary artery. The pulmonic orifice was markedly dilated. It measured 7.5 cm. in circumference. The wall was slightly thickened and the intima roughened. The leaflets were thin, but definitely thickened at the corpora aranti. There was a pedunculated globular nodule 2 mm. in diameter on the corpora aranti of the anterior leaf.

"The left auricle was moderately dilated and slightly hypertrophied. At the junction of the right and posterior walls was an area 1 cm. in diameter where the endocardium was covered by a shaggy fibrinous layer.

"The mitral valve was represented by a funnel-shaped structure, at the lower end of which was a circular orifice 5 mm. in diameter. There was a layer of fibrin along the line of fusion of the thickened leaflets. There were no recent vegetations. The chordae tendinae were markedly thickened and shortened: the leaflets almost fused directly with the small papillary muscles.

"The left ventricle was small, not dilated nor hypertrophied.

"The aorta was distinctly hypoplastic, measuring 4 cm. in circumference. It was very elastic and presented no atheromata. The aortic valve was negative, except for a few thin, flattened, translucent vegetations along the line of closure of the left posterior leaflet.

"The myocardium was glazed, watery, and showed a slight degree of fibrous scarring about small vessels.

"The coronaries were dilated and thin walled throughout."

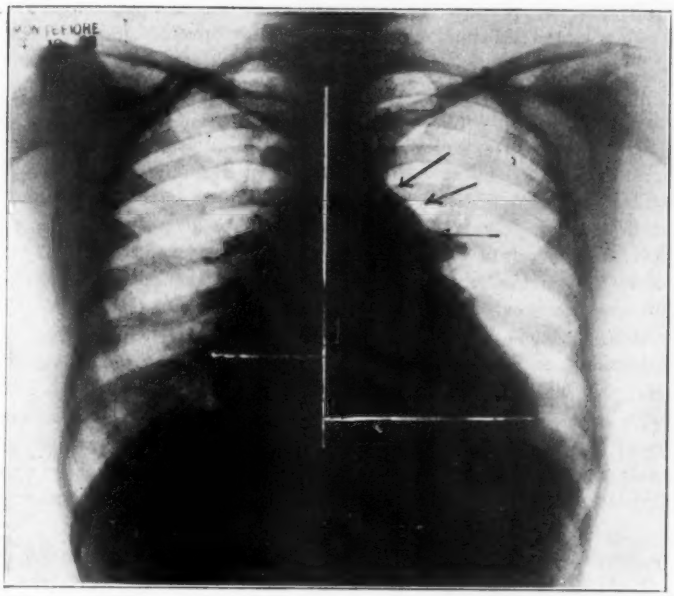

Fig. 3.—(Case 53289.) The heart shows enlargement of all chambers. M. R. 4.7 cm.; M. L., 12.2 cm. Note the marked bulging of the pulmonary artery.

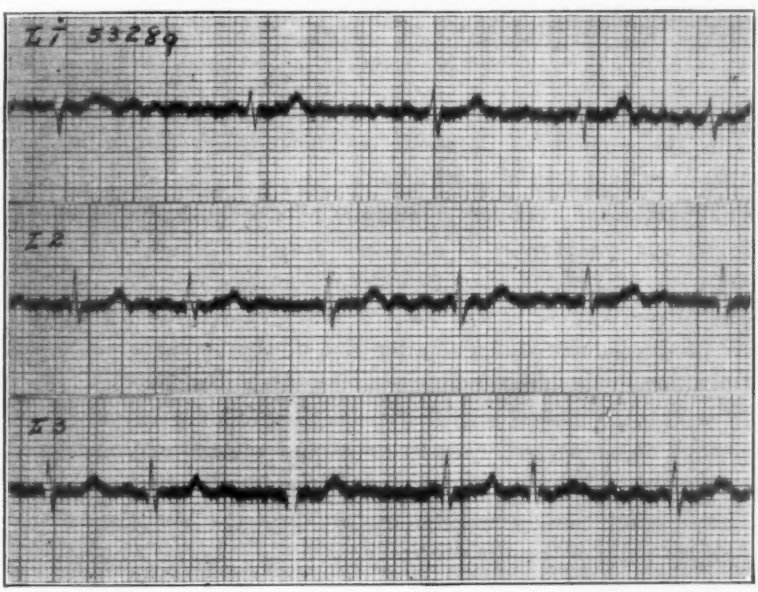

Fig. 4.—ECG. shows right ventricular predominance. Low voltage. Auricular fibrillation. Occasional premature beats of the ventricle.

Case 3.—No. 53289. A female, aged thirty-nine years, was admitted to the medical service on April 8, 1926. Her chief complaints on admission were swelling of the legs and shortness of breath of seven years' duration.

She had had acute articular rheumatism fifteen years prior to admission. Seven

years ago she began to note that she tired easily and that her legs swelled at times. Five years ago she was informed that she had heart trouble. Since then she had been in bed on and off for the symptoms which she presented on admission.

Physical examination revealed a slightly dyspneic individual with moderate cyanosis of the lips and distention of the superficial veins of the neck. The apex beat was in the fifth intercostal space, 13 cm. from the midline. The left border of the heart in the second intercostal space was 6 cm. from the midline. There was an inconstant thrill at the apex and a moderate diastolic shock over the pulmonic region. A short systolic murmur followed by a constant rougher diastolic murmur was heard over the apex. An inconstant diastolic murmur was heard over the second intercostal space to the left when the patient was placed in a sitting posture. The pulmonic second sound was accentuated. The pulses were unequal and irregular. There was a pulse deficit of 22. The blood pressure was 104/66.

The lungs showed moderate moisture at both bases and the liver was 6 cm. below the costal margin. The blood Wassermann reaction was negative.

Fluoroscopic examination with the patient in the anteroposterior position showed an enlargement of the heart in all directions. The aortic button was invisible and the pulmonic artery was markedly dilated. This showed up especially well in the first oblique position. There was no forcible pulsation of the artery in any of the positions.

Roentgen examination of the chest showed the heart to be markedly enlarged, involving all chambers. The pulmonary artery bulge was accentuated. Cardiac dimensions were M. R. 47. M. L. 12.2. (Fig. 3.)

The electrocardiographic tracing showed right ventricular predominance, a low voltage in all three leads, auricular fibrillation and an occasional premature beat of the ventricle (Digitalis?). (Fig. 4.)

CONCLUSIONS

1. The roentgen examination of three cases of mitral stenosis accompanied by the murmur of pulmonic insufficiency revealed dilatation of the pulmonary artery in all positions.

2. The particular type of dilatation of the pulmonary artery in mitral stenosis was found in all cases presenting the Graham-Steell murmur.

3. The lower voltage of the electrocardiograms showing right ventricular predominence and a smaller size of the T-waves helps to differentiate these cases from congenital lesions of the heart.

4. In combined cases of mitral stenosis in which aortic and pulmonic insufficiency is suspected, radiographic and electrocardiographic examinations are of value in eliminating the aortic lesions.

5. The characteristic roentgen picture and the electrocardiograph are of great help in the diagnosis.

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TRANSIENT AURICULAR FIBRILLATION IN ABDOMINAL DISEASES

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TRANSIENT or paroxysmal auricular fibrillation is more frequent than is generally supposed. The attack may be so brief and evanescent as to escape detection, and at such time can be identified accurately only by means of the electrocardiogram. On the other hand, the attack may last several hours or days, and then cease spontaneously. In the majority of cases no exciting cause can be ascertained. It is a cardiac disorder that has been most frequently associated with organic heart disease and toxic states, especially exophthalmic goiter and acute infections. Then again, it may be found in entirely normal individuals.

In this communication we desire to draw attention to another group of cases that seems to us to indicate an intimate relationship between acute abdominal conditions and transient auricular fibrillation.

There is very little to be gleaned from a study of the literature relative to this question. Some of the older writers merely mention that irregularities of the pulse, such as changes in rate and extrasystoles, may occur with gallstone colic and gastrointestinal disorders. Hoppe-Seyler[1] remarked that "The irregularity of the pulse sometimes observed may be due to involvement of the vagus system, by which an influence is exerted by reflex action on the heart." Umber[2] noted that at the onset of an attack of colic, because of the severe pain, the heart may be functionally disturbed through the sympathetics. Acceleration and irregularities of the pulse may therefore follow. MacKenzie[3] wrote that indiscretion in food and drink may readily induce extrasystoles.

It is surprising to note that the association of an absolutely irregular pulse and abdominal disorders has escaped notice heretofore. Very Recently Hamburger and Straus[4] made an electrocardiographic study of four cases of gall bladder disease associated with extrasystoles. In one of these cases they recorded a short paroxysm of auricular flutter. These patients showed no evidence of cardiac involvement. It appears from their observation that with the surgical removal of the pathological condition, some of these irregularities disappeared. Wolferth,[5] in a paper discussing intermittent auricular fibrillation, casually mentioned the case of a young man admitted to the University Hospital with an acute appendicitis, who developed a transient auricular fibrillation.

We have had the opportunity of observing clinically and electrocardiographically cases of auricular fibrillation occurring in diseases of the gall bladder, acute appendicitis, gastric ulcer during the stage of recurrence and finally in a case of extensive postoperative intra-abdominal adhesions.

CASE REPORTS

CASE 1.—Mrs. E. H., a German housewife, sixty-five years old, came under our observation in 1915. Her past personal history was negative except that she had had an epithelioma of the scalp for one year. This was finally cured by means of x-ray treatments at the Mt. Sinai Hospital during 1916. She complained of attacks of severe abdominal cramps referred to the right hypochondrium. The first attack dated back ten years. These attacks would reappear at intervals of from one to two years. During the period of remission the patient was absolutely symptom-free, but immediately following the cessation of an attack she would experience severe palpitation. The first attack of gallstone colic which we observed occurred in the spring of 1917. This was typical, associated with vomiting and a tender, acutely distended gall bladder. She had a slight fever and required a hypodermic injection of morphine. The painful seizure lasted for two or three days. On the fifth day while convalescing, she suddenly complained of feeling faint and was aware that her heart was beating very rapidly. When seen the pulse was found to be extremely irregular, 140 per minute with a well marked pulse deficit. She looked pale, anxious and very much alarmed. Morphine and digifoline were given hypodermatically. Tincture of digitalis in 2 c.c. doses was ordered to be given every three hours. Six hours later the pulse was regular, 80 per minute, and the patient was perfectly comfortable. During the following nine years and until her final illness in October, 1924, she had three such spells of gallstone colic, each followed during the stage of convalescence by a period of auricular fibrillation, which would cease either spontaneously or after the administration of digitalis. During the interim she was perfectly well and was able to perform her household duties with ease. She never complained of any cardiac symptoms. She was seen at frequent intervals, and the pulse was always found to be normal in rate and rhythm. The blood pressure averaged 160/90. Electrocardiograms taken during periods of remission showed a normal rhythm and a slight left preponderance. Her final attack occurred in 1924, and was more severe than any of her previous ones. There was continuous fever ranging from 100° F. to 103° F., lasting about a week. Examination revealed, aside from the jaundice, a large, distended gall bladder. This was exquisitely tender to pressure. With this there was nausea and vomiting. Morphine was given for relief of pain. During the second week of her illness the symptoms began to subside. The jaundice became visibly diminished and the stools gradually lost their clay color. Towards the end of the second week of her illness she suddenly developed an irregular tachycardia, typical of auricular fibrillation. Digitalis was administered in a similar manner given her in her previous attacks (2 c.c. every three hours until the physiological effect of digitalis had taken place). Whereas in previous attacks the drug had been effective, on this occasion after three days use the heart continued its rapid and irregular rhythm. Quinidine therapy was then instituted (0.2 gm.—gr. iii) every three hours. In about twelve hours the pulse showed a remarkable change. It became perfectly regular, beating at the rate of 180 per minute (auricular flutter). In spite of the continued use of quinidine for two more days, the tachycardia persisted. Her condition became alarming. Slight edema occurred in the dependent portions of the body. Quinidine was then discontinued. Digitalis therapy was

again instituted. The following day the fibrillation reappeared. This continued for two weeks until her death from bronchopneumonia complicated by a severe cystitis.

CASE 2.—Mrs. R. S., aged fifty-four years, housewife, was first examined Jan. 9, 1923. She complained of agonizing pain in the upper right quadrant of abdomen, associated with nausea and occasional vomiting. This pain was referred to the back and lasted until relieved by a hypodermic injection of morphine. During and immediately following this attack, she complained of faintness and palpitation. When first seen the physical examination revealed nothing but a slightly palpable gall bladder, associated with slight rigidity and moderate tenderness in the right hypochondriac region. About one month later, the patient experienced another attack of apparent biliary colic. Examination at this time revealed in addition to the above mentioned findings, a definite auricular fibrillation, which was corroborated by the electrocardiographic records. Quinidine was given, but had to be stopped, owing to the occurrence of palpitation and dyspnea. The electrocardiogram now showed an impure auricular flutter. Digitalis was then administered. The irregularity lasted about ten days before returning to normal rhythm. There was another attack of colic two months later, again associated with auricular fibrillation, which lasted for one week. Three months later she had another attack, together with a recurrence of auricular fibrillation. The patient has now remained free from attacks for three years. The cardiac rhythm remains normal, x-ray examination of heart is negative, and the electrocardiogram is normal.

CASE 3.—Mrs. B. S., thirty-four years old, housewife, complained of severe pain in the right hypochondrium, which began six months before we saw her. In September, 1926, she gave birth to a full-term child. The delivery was normal. There was severe vomiting through the entire period of gestation. She has had two attacks of colic during the past six months. There was slight glycosuria and pruritus also. On November 4, 1926, she was suddenly seized with a sharp, severe pain in the right hypochondriac region, transmitted to the angle of the right scapula and shoulder. The pain was severe and associated with nausea. She vomited once. Examination revealed the presence of an auricular fibrillation and a faint systolic blow, heard at the apex. The apex rate was 132, while the pulse at the wrist was 100 per minute. The abdomen was slightly distended. There was exquisite tenderness over the gall bladder, which was palpable and moved with respiration. Morphine and atropine sulphate were given by hypodermic injection and repeated in two hours. The following day the patient was free from pain. The pulse at the wrist and apex was 60, and regular except for an occasional extrasystole. The faint systolic murmur was still present. Twenty-four hours later the heart was regular and the other findings were the same as noted on the day previously.

COMMENT

The similarity in these three cases is very striking. The first two patients were observed for a sufficiently long time to determine definitely that the numerous attacks of irregularity occurred only during or immediately following the acute gall bladder attacks. Their association was therefore not a mere coincidence. On the contrary, it seems certain that there existed a definite relationship between the acute illness and the disturbance of the cardiac rhythm. It is also of great interest to note the action of quinidine in these cases. Instead of the prompt restoration of the normal mechanism, an auricular flut-

ter ensued. This disturbance may possibly have contributed towards the fatal outcome in Case 1.

CASE 4.—H. R., aged fifty-two years, male, merchant, came under observation on November 27, 1924. His family and past personal histories are of no significance. He complained of epigastric pains of a "pressing" nature, referred to the back and right side of abdomen. He also suffered from frequent sour eructations and pyrosis. The symptoms dated back for a period of ten years. These occurred at irregular intervals and lasted about one to two months. They were definitely related to the intake of food and appeared within two or three hours after meals. He was temporarily relieved by food, drink and alkalis. The longest remission lasted for one year. For the past eighteen months he had had attacks of palpitation, which came on very suddenly. They were usually associated with severe symptoms of epigastric distress. The palpitation lasted from one-half hour to a day. During such times he felt very weak and experienced a sensation of fainting. There was no nausea or vomiting. On physical examination he revealed the following positive findings: Slight thickening of the radials, and a blood pressure of 140/100. There was tenderness just above the umbilicus, which extended somewhat to the right. There was a Head zone corresponding to the areas of the fifth dorsal to eighth dorsal vertebrae, limited to the left side. The total gastric acidity was 76 units, free HCl 56, combined 16, and acid salts 8. There was no occult blood. The gastroenterological roentgen examination revealed a constant irregularity in the prepyloric region, with a slight six hour stasis.

He was placed on a modified Sippy diet and alkalis with subsequent rapid improvement. On December 11, 1924, he returned complaining of palpitation which began suddenly that morning. Examination at that time revealed a typical auricular fibrillation, confirmed by the electrocardiogram. A record made previously had showed normal curves except for a slight left preponderance. During the following two weeks he suffered repeated attacks of palpitation, recurring every day or two and lasting from one-half hour to a day or more. These would cease spontaneously and then return again. He was entirely conscious of their presence and could immediately tell when they abated. He was generally uncomfortable and became short of breath during the more severe and prolonged attacks. As soon as the attack had disappeared he was entirely free from symptoms. He was given quinidine sulphate 0.2 gm. (gr. iii) every three hours. After the second dose the attack ceased. Quinidine was continued, 0.165 gm. (gr. ii) twice daily for a month. He was free from attacks until March 3, 1926, when the gastric symptoms reappeared, together with the auricular fibrillation.

CASE 5.—I. S., a woman, thirty-eight years old, came under observation March 24, 1926. She had chorea at the age of twelve years, following which she developed evidences of mitral stenosis. She has been very active and occupied a responsible and exacting position as sales-manager. For about one year she complained of attacks of pain in the right lower quadrant of the abdomen. These pains occurred at irregular intervals, and were always associated with palpitation and distress about the heart. An electrocardiogram taken six months previously, during one of these attacks, showed the presence of an auricular fibrillation. She was given digitalis and improved. Two months later another electrocardiogram was taken, and a normal rhythm was found. When seen March 24, 1926, she presented signs and symptoms of a subacute appendicitis. The pulse was rapid and irregular, with a pulse deficit. She also complained of palpitation and cardiac distress. Electrocardiograms taken at this time revealed an auricular fibrillation of a coarse variety. She was immediately given quinidine sulphate and after four doses the palpitation ceased and the pulse became regular. The following day, because the symptoms and signs of appen-

dicitis increased and the temperature rose, an appendectomy was performed. Quinidine was continued throughout her stay at the hospital and she made an uneventful recovery. During the following eight months there were no further recurrences of palpitation. She regularly attends to her business as heretofore, and both her heart examination and electrocardiograms reveal a normal rhythm.

CASE 6.—I. C., thirty-six years old, male, peddler. On September 7, 1923, he complained of abdominal pains, occurring intermittently, and associated with oppression in the region of the heart. Ten years before the patient was operated upon for an acute gangrenous appendicitis at the Brooklyn Jewish Hospital, New York. Following this he developed multiple abscesses including a liver abscess, a subdiaphragmatic abscess, and a pleural empyema. These were all opened and drained. After a very stormy convalescence of seven months, the patient was discharged as cured. He remained free from any symptoms for about three years. He then began to complain of attacks of abdominal pains associated with some degree of nausea, a feeling

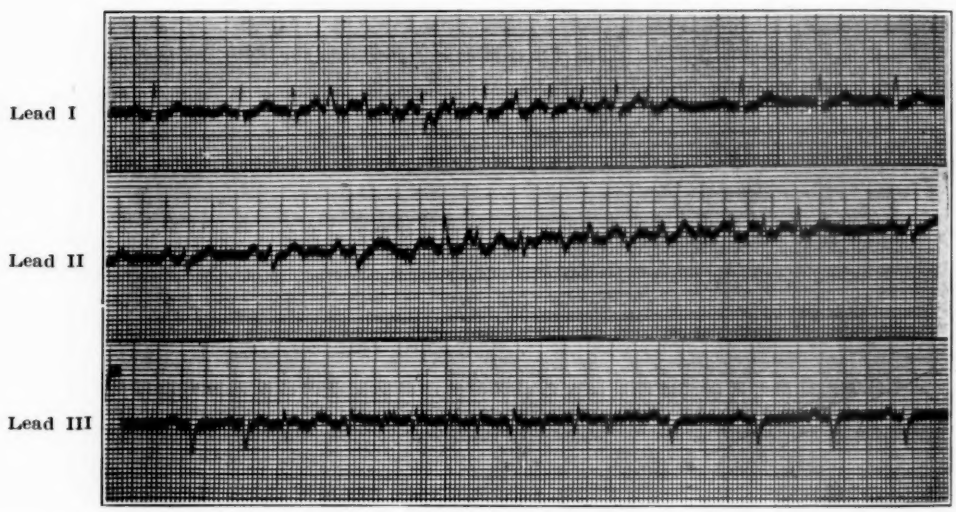

Fig. 1.—Electrocardiogram of Case 6. The interesting feature is the brief periods of fibrillation, in each lead, which come and go. Such evanescent paroxysms of fibrillation can be definitely determined only by means of the electrocardiograph.

of faintness, cardiac distress, and palpitation. Repeated examinations revealed nothing but the scars of previous operations. On March 8, 1926, he complained of severe abdominal pains and annoying palpitation, the latter occurring every few minutes during the past few days. He stated that he felt as if he were about to faint, the sensations coming and going every few seconds. Examination revealed nothing, aside from the previous findings, except for a very peculiar action of the heart. There were about 15 regular beats at about the rate of 80 per minute, then the pulse became extremely irregular and rapid. There was actually a delirium cordis. This lasted about 10 or 15 seconds, when the regular rate continued for 15 to 20 beats, followed by the return of the irregularity. He was always aware of these changes. An electrocardiogram was taken and showed alternate periods of normal rhythm, followed by impure flutter and fibrillation. He was given 0.3 (gr. v) of quinidine sulphate during the attack. On March 31, 1926, he again complained of a similar attack and after two doses of quinidine sulphate he was entirely free from symptoms. He continued the quinidine 0.2 (gr. ii) twice daily. The irregularity was controlled. The patient stated that he can provoke an attack by indulg-

ing in greasy foods, which induce "indigestion." On July 6, 1926, he again had frequent attacks of tachycardia, but then quinidine had no effect. When last seen on September 26, 1926, he informed us that he had no attacks for the past six weeks, because he had carefully observed his diet. There were, however, occasional extrasystoles. Electrocardiograms taken on this occasion revealed a normal mechanism.

DISCUSSION

In analyzing the cases above described, we are at once struck by the fact that the paroxysms of auricular fibrillation occurred only during the acute stages of the abdominal disorders. Five of the six patients were observed for a period of from one to nine years. It was fully established that the cardiac arrhythmia took place only during the acute stages of the intraabdominal disease. It was natural, therefore, to conclude that this was not a coincidence, but that a direct relationship existed between the incidence of the arrhythmia and the acute abdominal symptoms.

How this change in the mechanism of the heart beat is induced is problematic. Our object is to lay particular stress upon the fact that in certain individuals auricular fibrillation may develop during the course of an acute intraabdominal disorder, such as cholelithiasis, cholecystitis, ulcer of the stomach, etc.

There is, however, some experimental and clinical evidence which is suggestive. It has been known for some time that certain poisons may induce auricular fibrillation in experimental animals, and clinically in man. Inhalations of chloroform and ether have been followed by auricular fibrillation in animals. Even in such experiments it cannot be foretold which animal will or will not develop this particular irregularity. Robinson[6] has recorded a case of transient auricular fibrillation in a healthy young man following the inhalation of hydrogen sulphide. Digitalis and alcohol have been known occasionally to induce a paroxysm. In infectious diseases such as pneumonia, and general disturbances in metabolism such as exophthalmic goiter and severe acidosis, auricular fibrillation has been seen as a complicating factor.

Similarly, in organic heart disease, arteriosclerotic conditions and myocarditis, auricular fibrillation is not uncommon. It seems, therefore, that an individual predisposition must exist; for only a small proportion of patients suffering from the above conditions show an auricular fibrillation.

In such susceptible persons various toxins acting as exciting agents may precipitate a circus movement within the auricular musculature. Lewis[7] and his coworkers have clearly indicated that disproportionate variations between the refractory and conduction phases of the auricular muscle fibers are the essential elements necessary for a circus movement. Electrical stimulation and toxic substances are capable of doing this in experimental animals. In this connection the results of

Carter, Andrus, and Dieuaide[8] are very important. They found that various types of arrhythmia, including circus movements, could be induced in a perfused heart by changing the hydrogen-ion concentration in the perfusate. Greene and Gilbert,[9, 10] likewise, caused arrhythmias in man by inducing a state of anoxemia.

From the above mentioned experimental and clinical data it is plausible to assume that toxins arising in septic foci within abdominal organs may so affect the auricular musculature as to set up conditions suitable for the initiation of a circus movement. It is important to note that the presence of an auricular fibrillation in itself is no contraindication to surgical intervention. This depends solely on the associated condition and upon whether or not there are signs and symptoms of cardiac failure. In fact, auricular fibrillation might be considered an added indication for operation; since the removal of the septic foci would eliminate the offending toxin and so tend to restore the normal rhythm.

It is our belief that in many cases of transient fibrillation occurring in healthy persons without any apparent etiological cause, a latent infection may be present somewhere in the body. We have seen cases of transient auricular fibrillation disappear permanently after tonsillectomies, appendectomies, etc. It is important, therefore, to make a thorough search, including the abdominal organs, for septic foci in all such cases.

The immediate management of these cases is that of auricular fibrillation in general. In some persons quinidine is efficacious, as seen in Cases 4 and 5, but in other individuals it may give rise to untoward manifestations, in the form of auricular flutter or even ventricular tachycardia. This is possibly due to some myocardial change which makes the heart more susceptible to the toxic action of the drug. Digitalis is always of great service and in sufficient doses frequently seems to restore the normal mechanism promptly. When an operation is contemplated, the patient should receive a preliminary thorough digitalization, and if the rhythm is not restored to normal, quinidine should be administered. This should be continued during convalescence, provided it succeeds in restoring the rhythm. Otherwise, digitalis should be employed for the same purpose.

CONCLUSIONS

1. The attacks of transient auricular fibrillation in the six cases described above were probably induced by a toxemia arising in septic foci within the abdomen.

2. In the absence of signs and symptoms of cardiac failure, auricular fibrillation in itself is no contraindication to operation.

3. Removal of the diseased organ is likely to be followed by a permanent disappearance of the arrhythmia.

4. Quinidine is occasionally valuable. In some patients it may induce untoward results and may prove dangerous.

5. Masked infections are possibly the etiological factors for many cases of auricular fibrillation occurring in apparently healthy individuals. Such foci should be sought for diligently and removed whenever possible.

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CARDIAC ASTHMA*

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AMONG the respiratory symptoms of heart disease certain types of breathing have been identified as of particular significance. Conspicuous among these is the condition called cardiac asthma. This term has been used rather loosely in the literature to denote a variety of forms of dyspnea that have since been more clearly characterized. The literature of cardiac asthma consists mainly of discussions of its physiological pathogenesis rather than of its clinical individuality. Heretofore, no group of cases has been brought together sufficiently distinctive for differentiation.

In this communication the attempt is made to distinguish the various forms of respiratory distress that occur in the course of heart disease, and to elucidate each form by carefully studied cases. There is presented also a condensed review of the literature and a clinical classification of the respiratory manifestations in heart disease, based upon our knowledge of their pathogenesis.

THE MECHANISM OF DYSPNEA

It is recognized that the respiratory system usually gives rise to the earliest symptoms in heart failure; and that respiratory distress in response to effort is often the earliest sign of heart failure.[1] The term dyspnea is applied when there is distress in breathing. The mechanism of its production is by way of the respiratory center in the medulla. The latter is extremely sensitive to a deficiency of oxygen or an excess of carbon dioxide in the circulating blood. It is also sensitive to toxic products produced in the body under special conditions, to non-volatile acids, such as lactic acid following exercise,[2] and to substances introduced into the circulation that increase the hydrogen-ion concentration in the blood.

Haldane and Priestly[3] have demonstrated that the rate and depth of breathing are regulated by the amount of carbon dioxide which reaches the respiratory center in a given time. Hyperpnea and dyspnea are common features in heart failure because of a deficient elimination of carbon dioxide, due primarily to a deficiency in the heart and a slowing of the circulation in the lungs.

Besides, the respiratory center is also receptive to peripheral stimulation from sensory nerves of the skin as well as from the nerve ter-

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minals in the heart muscle and in the lungs. It may be affected by changes in intracranial pressure or by vascular disturbances in its vicinity. Haldane[4] states, "It is not the heart nor the bulbar nervous centers which govern the circulation rate, but the tissue as a whole. The heart and vasomotor system are only the executive agents which carry out the bidding of the tissues, just as the lungs and nervous system do in the case of breathing."

Hyperpnea, or air-hunger, implies an increase in the rate and depth of respirations.

With orthopnea the patient assumes the upright position of the trunk, any attempt to lie down being immediately followed by an increase in respiratory distress. It is attributable to resistance to the full pulmonary ventilation offered by the abdominal contents pressing against the diaphragm. The hydrostatic effect of the erect posture on the blood content of the abdomen and the peripheral vessels is also a factor. The frequent occurrence of simple periodic breathing at night is probably to be explained by the orthopnea due to the recumbent position.

Periodic or paroxysmal dyspnea is of various types and presents different degrees of severity. It occurs in a variety of conditions and apparently results from some specific stimulation of the respiratory center. The literature is now replete with discussions of this type of breathing and the term has assumed a generic amplitude to include Cheyne-Stokes breathing and the attacks of air-hunger that occur with myocardial disease.

CLASSIFICATION

It will thus be seen that the respiratory symptoms in cardiovascular diseases may result from four entirely distinct mechanisms:

1. Stimulation of the respiratory center by toxic products, excess of carbon dioxide, or nonvolatile acids in the systemic circulation.
2. Irritability of the respiratory center from a deficiency of oxygen due to impaired circulation—deficient transference of blood mass.
3. Nervous-reflex mechanism from a lesion in the myocardium or aortic-coronary area, as well as from peripheral pain.
4. Intracranial alterations of pressure or disease of the cerebral vessels.

Corresponding to these mechanisms different forms of respiratory distress may be induced. These may be classified as follows:

1. Of Pulmonary Origin.
   a. Congestive or simple mechanical dyspnea.
   b. Attacks of stasis or pulmonary asthma.
   c. Pulmonary edema.

2. Of Cardiac Origin (Spontandyspnoe or Grosskreislaufdyspnoe of Wassermann).[5]
   a. Paroxysmal or spontaneous dyspnea.
   b. Cheyne-Stokes breathing.
   c. Cardiac asthma.
   d. Uremic asthma.
3. Of Cardio-Reflex Origin.
   a. Cardiac asthma with angina pectoris, coronary thrombosis, and myocardial degeneration.
4. Of Cerebral Origin.
   a. Periodic dyspnea with intracranial disease.
   b. Cerebral arteriosclerotic asthma.

There are two conditions, quite individual in their pathogenesis, that have been confused in the literature under the name "cardiac asthma." In one of these (Group 1 above), the symptoms are essentially those of pulmonary congestion associated with attacks of dyspnea and wheezing, brought on often after exertion. The other forms of "cardiac asthma" (Groups 2 and 3 above) depend upon factors in the arterial side of the circulation, i.e., upon the left ventricle and its ability to maintain adequately the respiratory center in normal condition of blood supply and oxygenation. The word "asthma" is derived from the Greek $\alpha\sigma\theta\mu\alpha$, meaning a gasping or short-drawn breath.

STASIS OR PULMONARY ASTHMA

In pulmonary stasis the origin of the dyspnea and dyspneic attacks is to be sought for solely in the pathological study of the heart. The organic conditions underlying its occurrence are usually stenosis of the mitral valve and the advanced valvular defect (tricuspid insufficiency) that develops with increasing heart failure. A history of longstanding chronic myocarditis, cardiac insufficiency, auricular fibrillation or auricular flutter, is often part of the picture in these cases. The mechanical embarrassment of the circulation in the lungs is usually associated with venous and liver engorgement. This form of cardiac dyspnea is obviously a more or less chronic condition. During its progress exacerbations frequently occur in the form of paroxysmal attacks. For these attacks I venture to suggest the term "pulmonary asthma."

Attacks of pulmonary asthma are characterized by their rapid, or more gradual, onset after strain or exertion beyond the patient's wonted capacity. The patient is compelled to rest seated or quiet in the recumbent position and shows both inspiratory and expiratory dyspnea, orthopnea, wheezing and a varying degree of cyanosis.

On physical examination there are wheezing, sibilant and moist

râles scattered over the lungs, usually with signs of congestion at the bases. The râles are both vesicular and bronchitic. There also is congestion of the liver and edema of the extremities. The vital capacity is in general much diminished and falls still further during the attacks of pulmonary asthma. The attacks may last only a short time, but often are much prolonged, for hours or sometimes days. They may gradually subside or, with increasing stasis, may end in pulmonary edema. Signs of valvular involvement are present, with accentuated pulmonic second sound. The pulse is usually rapid, small, compressible and is often completely irregular. The blood pressure is low both in the intervals and during the attacks. There is usually also an increase in the venous pressure, often with distension of the larger veins. Oxygen is of considerable benefit in these cases.

Pathogenesis of Stasis or Pulmonary Asthma and Pulmonary Edema.—Mitral stenosis and advanced chronic myocardial disease represent that form of circulatory disturbance in which the pulmonary circulation is overladen. As the dilatation of the pulmonary capillaries increases, the respiratory and vital capacity of the lungs is encroached upon, producing a constant predisposition to dyspnea. The pressure in the pulmonary artery increases. Finally, the dynamics of the right side of the heart are disturbed, and the venous system begins to contain more blood. The frequency of hemoptysis even in early mitral stenosis is clinical testimony to the fact that over-filling of the pulmonary circulation has taken place.

The question of increased pressure in the pulmonary capillaries should be dismissed from consideration as not characteristic of pulmonary stasis. It has elsewhere been shown that a diffuse or compensatory dilatation of the pulmonary capillaries takes place in response to mechanical obstruction to the outflow of blood from the lungs. Lichtheim[6] showed that experimental constriction of the aorta to a marked degree produced no increase of pressure in the lesser circulation. Recently Drinker, Peabody and Blumgart[7] found in their "observation on cats in which the pulmonary veins were obstructed, that a high degree of pulmonary stasis may be produced without causing much actual increase in pulmonary blood pressure." Capillary dilatation naturally produces a diminished vital capacity. Wassermann[8] suggests that when pulmonary edema occurs in these cases, it is associated with tricuspid insufficiency and right heart failure.

PAROXYSMAL CARDIAC DYSPNEA—CARDIAC ASTHMA

Quite in contrast with pulmonary asthma, the main conditions in which spontaneous or paroxysmal dyspnea occurs are the aortic lesions and coronary arterial disease. The commonly associated

lesions are those of arteriosclerosis, hypertrophied heart with hypertension, pulmonary emphysema and chronic interstitial nephritis—all evidence of extensive arterial change. Any valve lesion may be present; aortic dilatation or actual aneurysm is not uncommon. All varieties of altered heart mechanism may be found. Pulsus alternans is especially frequent. Anginal pains are often present. Cardiac asthma is relatively frequent in the later phases of aortic insufficiency but is rarely met with in mitral insufficiency or in uncomplicated mitral stenosis.

Paroxysmal dyspnea is often associated with a disturbance in the acid-base balance of the blood and is a frequent symptom in cases of so-called cardiorenal disease in which the eliminative and metabolic capacities are disturbed. In the more recent literature, the term paroxysmal dyspnea includes hyperpnea due to central anoxemia, Cheyne-Stokes breathing, and cardiac asthma.

Kreysig[9] first differentiated the continual dyspnea of cardiacs from the attacks of paroxysmal dyspnea that occur with a sense of suffocation. He mentions the occurrence of these attacks at night, marked by a feeling of anxiety and by absence of any congestive signs. Hope[10] later emphasized this distinction, dividing the asthma into "moist," in which there is pulmonary congestion as in mitral stenosis and which I have designated "pulmonary asthma"; and "dry," if the pulmonary stasis is only temporary or terminal, as in advanced chronic myocarditis. Zehetmayer[11] also distinguished between a continued and a paroxysmal dyspnea. Since then the name cardiac asthma has been associated with the latter type.

The following are classical descriptions of attacks of cardiac asthma:

"The patient may have gone to bed in his usual health and after three or four hours' sleep he is awakened with a feeling of suffocation, and an intense desire to breathe deeply. He sits up in bed and breathes in deep and labored fashion. A sense of great prostration may add to his suffering. Wheezing sounds may appear in the chest; he may cough up some frothy phlegm. The attack may last for half an hour or longer; then the breathing becomes quieter and he is able to lie down, though he keeps starting up and finally assumes a position with his head and shoulders raised, passing the remainder of the night in uneasy slumber. Once these attacks begin they are apt to continue and the nights of the patient often become periods of great distress."[12]

In a discussion of interesting biochemical factors, Lewis states:

"There are patients, usually elderly, who suffer from urgent dyspnea. The breathing is laboured; it is periodic and of the Cheyne-Stokes type. The patients are not orthopneic, they exhibit few signs of venous or liver engorgement; pressure upon the abdomen does not materially increase the depth or rate of respiration. The uncomplicated cases are not cyanosed. The blood is fully aerated and has a low tension of carbon dioxide. There is little or no reserve. The administration of oxygen affords practically no relief. A conspicuous feature is the presence of nocturnal attacks of breathlessness, and these wake the patients repeatedly from slumber, are often suffocative and last from a few minutes to half an hour or more. The heart

is a little dilated; the pulse rate is almost always increased (80-100) and especially towards evening. The temperature is generally subnormal. The blood after removal of its carbon dioxide shows considerable decrease of alkalinity, which is due to the excessive presence of nonvolatile acids or acid salts.[13]

"The class of case which shows this condition most characteristically is the elderly person and those who suffer from arterial and cardiosclerosis. They frequently have a high blood pressure, and the heart is usually regular except for the presence of occasional or frequent extrasystoles. In these cases, we sometimes find the best examples of the pulsus alternans. In most cases this symptom is a very grave sign and usually indicates an exhaustion of the heart so extreme that only a very slight improvement can be hoped for, especially when associated with pulsus alternans and other signs of heart exhaustion. Similar attacks of breathlessness occur at the end of the apneic stage of Cheyne-Stokes respiration."[12]

We may add that in every case of cardiac asthma, there is evidence that dyspnea on exertion has existed for some time preceding the sudden attacks of asthma. Attacks of angina pectoris or coronary thrombosis are often recurrent in these cases.

The onset of the attacks is sudden, the face pale, and the distress great. Cardiac asthma may be the first sign of heart failure; it may come on after excitement, a meal, the slightest extra exertion, or without any adequate reason. During the attack, the pulse is usually full and of high tension; the blood pressure increases as well as the rate of circulation, mainly as an effect of the muscular efforts induced by dyspnea. In paroxysmal dyspnea pulmonary hemoptysis is not usual.

On physical examination the signs of congestion are often absent but there may occur a tracheobronchial wheezing. The great pallor during the attacks is due to stimulation of the vasomotor center.

Pathogenesis of Cardiac Asthma.—The pathogenesis of cardiac asthma is still in debate. The predominant features of myocardial insufficiency or coronary involvement are an essential and all-important part of the picture. Without marked myocardial deficiency, cardiac asthma cannot be assumed to be present.

Traube[14] asserted that pulmonary stasis is the main cause of this condition. He admitted, however, the possibility that an increase in the carbon dioxide of the blood occurs and must be called upon to account for the occurrence of the attacks during the night. Von Basch[15] assumed that it was the turgidity of the pulmonary capillaries which diminished the expansibility of the lungs and so induced the attacks of asthma. Most authors have assumed a direct relation, a sort of balancing, between the systemic and pulmonary circulation, and have conceived of cardiac asthma as occurring with pulmonary stasis due to weakness of the left ventricle. From the features of the attack and its association with coronary disease, Krehl[16] supposed that the attacks were due to temporary weakness of the left ventricle and

to some increase in pressure and loss of velocity of the blood in the lungs.

Von Leube[17] states that under conditions in which the heart, especially the left ventricle, rapidly weakens, there occurs a sudden increase in the pressure of the pulmonary capillaries in individuals who, owing to contracted kidneys, arteriosclerosis, cardiac defects, lipomatosis, etc., incline to dyspnea. A greater filling of the left auricle and of the capillaries of the lungs will occur if suddenly a new demand upon the activity of the left ventricle is imposed. The consequence will be its weakening and dilatation, which is more apt to occur the more the nutrition of the heart has become deficient; an attack of dyspnea is the natural consequence, an event which takes place frequently in sclerosis of the coronary artery.

In recent years the subject has received careful study from the biochemical side, in England, and has been studied exhaustively from the clinical side by Wassermann.

Wassermann[18] presents as his thesis the conception that cardiac asthma is a form of spontaneous dyspnea which occurs in paroxysms and is due to a deficient arterial systemic circulation producing a central anoxemia. This is the crucial cause of the dyspnea. He uses the term "Spontandyspnoe or Grosskreislaufdyspnoe" (circulatory or spontaneous dyspnea) in a generic sense to cover the group of conditions in which the dyspnea is sudden in its onset, usually at night, spontaneous in its origin, paroxysmal in its recurrence, and, in the usual attack, does not go on to pulmonary edema. In this condition he also includes all forms of paroxysmal dyspnea, as well as Cheyne-Stokes breathing. Wassermann dismissed the theory of pulmonary stasis from consideration in the production of this form of attack.

Cardiac asthma, according to his idea, is essentially a respiratory center phenomenon, the result of increased sensitiveness of the center, produced by prolonged anoxemia. The fact of the occurrence of the attacks at night lends weight to this conception, in that sleep also depresses the sensitiveness of the respiratory center. In consequence the anoxemia can go for a long time before the patient is suddenly awakened with a severe attack in which the "oxygen debt," as Hill terms it, is very great.

The sequence of events, therefore, in the production of the attacks of paroxysmal dyspnea is as follows: The stimulus reaches the respiratory center through the arterial circulation; the center reacts in a specific way by a peripheral stimulus to the lungs; dyspnea develops, increasing the pulmonary ventilation and the heart rate. As a result, the irritability of the respiratory center lessens and the paroxysm of dyspnea subsides. If the ventilation of the lungs is

inadequate, the dyspnea increases, at the same time stimulating the adjacent vital centers, particularly the vasomotor and vagus.

The vasomotor effect is a constriction of the peripheral arterioles producing pallor of the skin, and forcing the blood on to the systemic venous circuit which in this way may become overloaded in cases of cardiac asthma. The vagus effect produces constriction of the tracheobronchial musculature, increasing the mechanical efforts to breathe, and this in turn accelerates the venous circulation.

The outcome of an attack may be twofold: If the aeration does not become adequate, paralysis of the respiratory center may result and death ensue. The second eventuality is heart failure, particularly evidenced by a falling blood pressure during the attack. The left ventricle dilates as a result of the continued peripheral resistance, producing finally also pulmonary stasis.[19]

Wassermann believes that pulmonary stasis or edema results only when there is definite dilatation of the left ventricle. He postulates the theory that the ventricular contraction forces the blood not alone into the aorta but back into the left auricle and also into the lung. This double pump mechanism, according to him, is an essential effect preliminary to the production of pulmonary stasis in these cases.

Dynamically the left ventricle serves two purposes: (1) The filling of the systemic circulation; and (2) its diastolic effect is that of relieving the pulmonary circulation. It is the distinction between these effects that separates what I have called "pulmonary asthma" from cardiac asthma. Wassermann believes that cardiac asthma is due to the propulsive weakness of the left ventricle.

From this it would seem that the respiratory center in these cases suffers from blood-want rather than from oxygen-want. The mechanism by which the attack subsides also implies this—the main effects of the attack being the transference of blood mass from the abdomen by vasoconstrictor action and by muscular movement.[20]

Morphine lowers the irritability of the respiratory center, making it less sensitive to anoxemia and to acute fluctuations in carbon dioxide (P_H) of the arterial blood.[21] Its efficacy in these cases supports the belief that the symptoms are of central origin. The value of nitroglycerin lies in the improvement of the cerebral circulation which results from widening of the intracranial vessels. Inhalation of carbon dioxide sometimes is beneficial, although the exact reason for the benefit is not known. The administration of oxygen in these cases does not give relief. Wassermann found no beneficial effects from venesection, although in one of his cases there is a note of distinct improvement following it.

CHEYNE-STOKES RESPIRATION

Mackenzie[22] came to the conclusion that cardiac asthma was in most cases merely an advanced stage of Cheyne-Stokes respiration, and that the attacks of asthma came on at the end of a long period of apnea.

Wilson[23] pointed out that there may be a common factor in the causation of Cheyne-Stokes breathing and cardiac asthma. It appears probable that in these cases the blood supply to the medulla is deficient, either from circulatory failure, arteriosclerosis, or increased intracranial pressure.

There are two distinct types of Cheyne-Stokes respiration. One is associated with increased intracranial tension and lessened cerebral circulation.[24] In this type, there is an increase of blood pressure and an acceleration of pulse rate during the period of hyperpnea, thus reestablishing the cerebral circulation; the fall of blood pressure with the resulting brain anemia is associated with the period of apnea and a slowing of the pulse rate. This form may also occur in normal individuals in high altitudes. In these cases, the phase of hyperpnea is associated with a rise of blood pressure and a slowing of the pulse.[25] The other type occurs in association with cardiovascular or renal disease, and in these exactly the opposite relation was found; during the period of hyperpnea, there was a fall of blood pressure and a slowing of the pulse and during apnea a rise of blood pressure and an increased pulse rate.[26]

RELATION OF ANGINA PECTORIS TO CARDIAC ASTHMA

Hoffmann[27] assumed, in addition to the above theories, a reflex neurotic element as a factor in the production of these attacks. Hoffmann and L. Hess[28] associate attacks of angina pectoris with changes at the mouth of the coronary artery. For a long time, cardiac asthma and coronary sclerosis were considered as closely related. Fränkel[29] noted the frequency of cardiac asthma in coronary disease. Rosenbach[30] asserted that the two conditions are independent. Wassermann found from his group of cases that an attack of angina pectoris, with coronary thrombosis, takes place first in these cases, producing left ventricular deficiency, and that attacks of cardiac asthma are a later development.

Attacks of angina pectoris and coronary thrombosis certainly stand in physiological relation to paroxysmal cardiac dyspnea. Francois Franck[31] demonstrated that there exists a reflex mechanism between the aorta and the respiration. He found that irritation of the heart or aorta produced reflex respiratory phenomena such as spasm of the larynx and bronchi which were intensified by the coexistence of a valvular lesion. In cardiac asthma, the attacks usually come on at night at the same time as some of the paroxysmal neuroses. Chvostek[32] be-

lieved that although cardiac dyspnea is of central origin, other stimuli may arise from an extensive lesion involving the myocardium and reflexly produce acute ventricular fibrillation and sudden cessation of the heart beat. From Wassermann's reports, the severe attacks of cardiac asthma resemble attacks of coronary thrombosis in which the dyspnea is the predominant symptom. These attacks come on mainly at night, with premonitory symptoms of anxiety, cold sweat, marked pallor, and especially angor animi, and are perhaps followed by slight cyanosis.

Mackenzie[33] says, "As a rule the patients that suffer from an attack of angina pectoris do not feel distress in breathing, although they may feel the chest constricted and have a desire to expand it. Some experience breathlessness only on certain efforts, as carrying a heavy bag upstairs; at other times they suffer from pain and constriction as well as breathlessness."

The dyspnea that is associated with angina pectoris can have two explanations: (1) That it is reflex in its mechanism, from the heart to the respiratory center and reflexly to the lungs; (2) that it is due to cardiac insufficiency. Wassermann[34] dismisses the first of these explanations on not entirely convincing grounds. Elsewhere the occurrence of paroxysmal dyspnea has been described as a prodromal manifestation of angina pectoris, in cases in which the myocardial changes were gradual and progressive.[35]

CEREBRAL ASTHMA

The relation of intracranial pressure to paroxysmal dyspnea is mentioned above in connection with Cheyne-Stokes breathing.

In some cases paroxysmal dyspnea has been ascribed to cerebral arteriosclerosis and has been called "cerebral asthma."[36] If cerebral arteriosclerosis were a frequent cause of paroxysmal dyspnea, other cerebral centers would be affected simultaneously and perhaps first, of which there is little evidence. Wassermann[37] believes that, if this be admissible as a cause of paroxysmal dyspnea, the functional deficiency of the left heart is a contributory factor in these cases.

DIFFERENTIAL DIAGNOSIS FROM BRONCHIAL ASTHMA

Pulmonary and cardiac asthma are shown to be distinct entities. They are in no way related to essential or bronchial asthma. They are well defined in their etiology, cardiac in their pathogenesis, distinct in their clinical picture, and entirely different in their prognosis and treatment from bronchial asthma.

The mechanism of pulmonary asthma is quite different from that of bronchial asthma. In the former, the constrictor element of the bronchial musculature is absent, while in the latter this must be assumed as the essential factor. In both the onset of the attack is rapid

and the respiration is generally retarded. In pulmonary asthma, the dyspnea is, corresponding to its pulmonary origin, mixed; i.e., inspiration and expiration are equally obstructed. In bronchial asthma, on the contrary, it is almost exclusively expiratory. In the former type the attacks are usually shorter in duration and are relieved by cardiac stimulants. Adrenalin, on the contrary, does not exhibit the magic efficacy that it does in bronchial asthma. Percussion in bronchial asthma as well as in pulmonary asthma shows an extension of the normal borders of the lungs; in the former affection, owing to the acute emphysema, in the latter in consequence of the distension and rigidity of the lungs.

In paroxysmal cardiac dyspnea the dilated heart is also in part covered by the rigid, distended lung, and according to the condition in which the heart was before the attack, the dullness will prove to be at times diffused, at others normal or diminished. While in bronchial asthma loud whistling respiratory râles and profuse moist râles always prevail, especially during expiration, these abnormal respiratory murmurs are absent in paroxysmal dyspnea, except when it terminally passes into pulmonary edema.

Bronchial asthma may, of course, complicate cardiovascular disease. Occasionally a patient with bronchial asthma will develop also pulmonary asthma or paroxysmal dyspnea in the course of his heart disease. In patients with circulatory disease it is most probable that the asthma is of cardiac origin. The fact that patients react by cutaneous tests to protein substances is no indication that the asthma is definitely bronchial. In one report of four cases grouped to show bronchial asthma as complicating cardiovascular disease, at least two were, from their description, cases of cardiac origin rather than of bronchial asthma.[38]

I have observed the two forms at different times in the same patient. It is most probable that uremic asthma is cardiac in type and pathogenesis.

Pulmonary asthma and paroxysmal cardiac dyspnea frequently coexist during the advance of myocardial degeneration. This fact, until recent years, obscured the clinical distinctness and the pathogenic individuality of each. In some of the case reports that follow, the association of pulmonary asthma with paroxysmal cardiac dyspnea is well illustrated.

CASE REPORTS

CASE 1.—Mrs. G. D., aged thirty-nine years, suffered from rheumatic pains for eight years. She had precordial and left dorsal pain after exertion, dyspnea, palpitation and weakness. For the past year she has had sudden attacks of cough, wheezing and hemoptysis, which recurred after excitement or exertion and were relieved by rest. These often continued for several days at a time both when the patient was awake and during sleep.

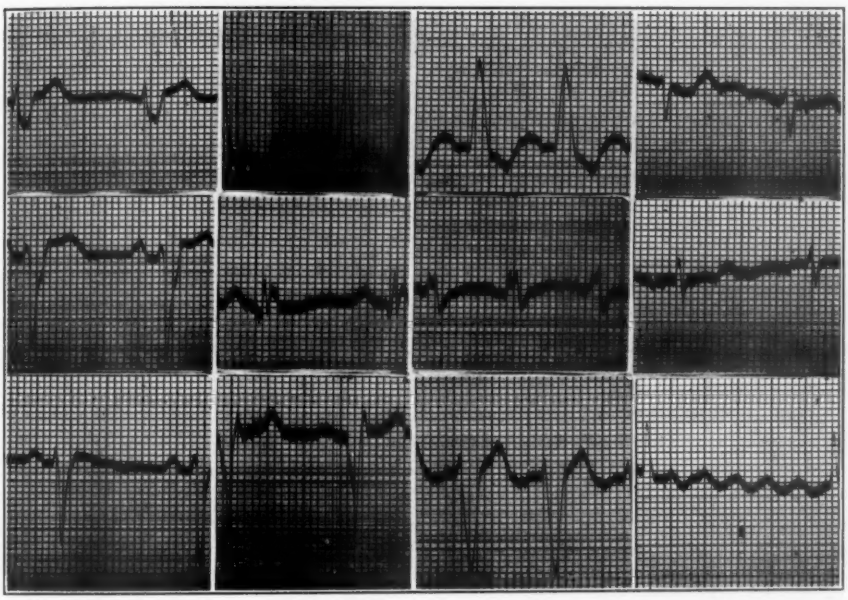
The heart showed mitral regurgitation and stenosis with accentuation of the pulmonic second sound. The blood pressure was 126/74. High-pitched and moist râles were found scattered over both lungs.

The patient improved remarkably under digitalis medication so that the lung signs cleared and the vital capacity increased.

Summary.—Rheumatic mitral regurgitation and stenosis; attacks of pulmonary asthma.

CASE 2.—Mrs. B. K., aged forty-two years, had mitral stenosis and auricular fibrillation. She has had periods of decompensation with moderate edema and pulmonary asthma for which she had to remain in bed for several days at a time.

In these attacks, she was slightly cyanosed. The heart was absolutely irregular but slow, with evidence of mitral stenosis. The lungs showed scattered moist râles and dry bronchitic wheezing. The liver was felt just below the free border and



Case 3 Case 10 Case 13 Case 2

Fig. 1.—Electrocardiograms in pulmonary and cardiac asthma.

there was moderate pretibial edema. The vital capacity was much below normal. The electrocardiogram showed right ventricular preponderance and auricular flutter which, under digitalis medication, changed to coarse auricular fibrillation. (Fig. 1.)

At one time she had a sudden attack of burning pain and a sense of vice-like compression across the lower chest which soon diffused upward, radiating to the left pectoral region and both scapulae. This lasted ten minutes and left her very weak for several hours. The pain recurred together with attacks of characteristic cardiac asthma with gasping breath, dyspnea, orthopnea, wheezing, cough, and expectoration lasting about one hour.

Summary.—Long standing mitral stenosis; auricular flutter; auricular fibrillation; repeated attacks of decompensation with pulmonary asthma; attack of angina pectoris, recurring together with attacks of cardiac asthma.

CASE 3.—A. G., aged sixty-seven years, had for three years asthmatic attacks which occurred after exertion, with marked dyspnea and slight cough. He also de-

veloped a burning pain across the middle and both sides of the chest, and a peculiar sensation of fear and tremulousness before the asthmatic paroxysms. In the attacks he panted for breath with a grunting sound.

The heart was obscured by emphysematous lung, and its sounds were not audible over the apex. The pulmonic second sound was louder than the aortic. There was a moderate arcus senilis and cyanosis of the mucous membranes.

The blood pressure was 128/82 and there was a pulsus alternans. The urine contained albumin and hyaline casts. The electrocardiogram showed marked arborization block and the QRS wave was widened to 0.14 of a second. (Fig. 1.)

Summary.—Senile arteriosclerotic myocarditis; prodromal anginal symptoms; cardiac asthma.

CASE 4.—J. S. M., aged sixty-five years, had an attack of coronary thrombosis five years before with acute pulmonary edema.

For two years he has suffered increasing dyspnea and at times slight cyanosis both of which are relieved by oxygen inhalation and rest. In these attacks, often for days, the patient reclines on pillows or in a chair slightly cyanosed, dyspneic, wheezing and coughing. Continuing his occupation which involved moderate strain, he has developed considerable edema of the feet and legs and a moderate degree of ascites, with the liver enlarged to four fingers below the free border. The heart is enlarged to the left, the first sound weak. There are no murmurs nor accentuations. The urine shows albumin and casts.

Often when just about to fall asleep, the patient awakes with a feeling of breathlessness for which he has to walk about or sit in a chair for perhaps fifteen minutes and then again attempts to sleep.

Summary.—Attack of coronary thrombosis with acute pulmonary edema, progressive myocarditis with attacks of pulmonary asthma and also nocturnal cardiac asthma.

CASE 5.—S. A., aged fifty-eight years, suffered for five years from slight dyspnea on exertion, momentary dizziness, and darkness before the eyes at times. In his occupation he walked stairs daily.

For three years, he had had occasional attacks in the early morning lasting fifteen minutes. In these he suddenly awoke with dyspnea, wheezing, slight cough, and expectoration. For periods he would have attacks almost every night. After moderate exertion during the day, he would suddenly begin to pant for breath, with wheezing, which symptoms were relieved by a few minutes of rest.

Physical examination showed marked arcus senilis, distended venules on the face and nose with moderate cyanosis. The heart was slightly enlarged to the left and more to the right. There was a systolic blow at the apex, less over the aortic area and marked ringing accentuation of the second aortic sound. The blood pressure was 206/94, without alternation. The lungs showed wheezing râles over the upper lobes and congestion of the bases. The free border of the liver was palpable and there was moderate edema of the feet.

Summary.—Attacks of cardiac asthma occurring during the night and after exertion during the day; hypertension; aortitis; dilated right heart.

CASE 6.—W. J. W., aged thirty-five years, had acute articular rheumatism and for twenty years involvement of the heart. He suffered little, however, until one year ago when he began to have a sensation of severe pressure across the precordium and upper sternal region. This occurred usually late at night, with marked difficulty in breathing, wheezing in the chest, dyspnea and tachycardia. Milder attacks occurred repeatedly after exertion.

Examination showed the left heart border in the anterior axillary line. There was

a diffuse heaving impulse of the entire precordium with a systolic thrill over the aortic area. Over the apex and precordium, there was a loud, rough, musical, systolic blow transmitted from the aortic area where it radiated to the vessels of the neck. There was the typical aortic diastolic blow over the sternum, with Corrigan and marked capillary pulse.

The blood pressure was 150/48. The electrocardiogram showed marked widening and notching of the QRS wave and high voltage.

Summary.—Rheumatic aortic valvular disease with aortic regurgitation; marked cardiac hypertrophy and dilatation; attacks of cardiac asthma.

CASE 7.—T. R., aged fifty-five years, suffered for three years from attacks of dyspnea after walking one block which compelled him to stop. He had upper sternal pressing and a feeling of heaviness in the forearm. A year and a half before the first examination, he had a severe attack of cardiac asthma which recurred several times.

His worst attack was observed when he arrived at my office after a long ride. He suddenly became breathless and stood continuously gasping, his face pale, eyes opened wide with a profuse cold sweat. This attack lasted about fifteen minutes. He had a dreadful feeling of anxiety, and dissolution seemed imminent.

His heart sounds were weak and he soon began to have signs of pulmonary congestion, and even edema. The blood pressure was 200/112 with marked pulsus alternans. Nitroglycerin seemed to increase the dyspnea and a moderate degree of cyanosis developed. A half grain of morphine produced fairly prompt relief. The blood pressure soon fell to 144/92, although the alternation remained very distinct. The liver was enlarged and he had moderate edema of the legs. His urine showed albumin and casts.

The electrocardiogram showed left ventricular preponderance. The QRS wave was notched and widened in all three leads.

The attacks of cardiac asthma recurred, and he was seen subsequently in very much worse condition with frequent pressing sternal pain and aching in the upper dorsal region.

Summary.—Attacks of sternal pressure for three years with increasing dyspnea; chronic nephritis; hypertension; pulsus alternans; chronic myocarditis; severe attacks of cardiac asthma.

CASE 8.—M. R., forty-six years old, gave a family history of "asthma." His father died of "asthma" at the age of sixty-five, and one brother and paternal grandfather died of "asthma." At the age of forty, after walking, he had a sudden attack of vice-like pain in the chest with a severe gripping pain in the left elbow. This lasted a few minutes and recurred often with a sensation of suffocation and air-hunger. During the night he would awake with attacks of compelling dyspnea in which he had to get out of bed and stand supported against a wall, gasping for breath. These lasted a few hours and sometimes the entire night. He had no wheezing during the attacks. Often, when the patient fell asleep he had typical Cheyne-Stokes breathing.

The patient had a sallow, pale complexion. His heart was enlarged both to the left and right, its apex seen and felt in the sixth space. At the apex, the sounds were weak and the first sound was of poor muscular quality. The pulmonic second sound was better audible than the aortic. Occasional ventricular premature beats occurred. The pulse was small and there was moderate cyanosis. The blood pressure varied between 102/90 and 98/64. The liver, with aggravation of the condition, became congested and extended down to the level of the navel, and moderate pretibial edema developed. The urine contained albumin and few hyaline and broad granular casts. The polygraphic tracings showed pulsus alternans.

The electrocardiogram showed low voltage, right ventricular preponderance; the P-wave high, wide and notched in Lead II; and the QRS wave was often of nodal origin and aberrant.

Summary.—Angina pectoris; chronic myocarditis; pulsus alternans; Cheyne-Stokes breathing; attacks of cardiac asthma.

CASE 9.—Mr. L. R., aged sixty-one years, had an attack of cerebral thrombosis at the age of fifty-six from which he gradually recovered. For the past year and a half, he has become fatigued after exertion, with extreme dyspnea, wheezing in the chest and slight cough. With these attacks, he suffers slight precordial pain, but no severe angina.

His heart is greatly enlarged both to the right and left. At the apex there is a rough systolic blowing murmur heard better over the aortic area and transmitted upward. There is also a rough diastolic short murmur over the sternum with marked accentuation of the aortic second sound. He has occasional ventricular extrasystoles. The blood pressure is 182/118, with pulsus alternans. His lungs show congestion of both lower lobes and he has at times Cheyne-Stokes breathing (Fig. 2). The liver is enlarged and there is a slight amount of ascites and marked edema of the lower extremities.

Summary.—Chronic myocarditis; hypertension; pulsus alternans; attacks of cardiac asthma and Cheyne-Stokes breathing.

CASE 10.—I. P., aged fifty-seven years, had attacks of severe distress in breathing, with pressing pain in the precordium and weakness, for a year and a half. The attacks occurred more especially during the night, lasting half an hour or longer, with asthmatic wheezing toward the end of the attack, and sweating, pallor, cyanosis, and pink-tinged expectoration. He later developed more typical anginal attacks with severe pain in the midsternum radiating to the left.

Physical examination showed the heart enlarged. A systolic blow was present at the apex which was also heard faintly over the aortic area. There was accentuation of the aortic second sound and marked tortuosity of the temporals. The blood pressure varied between 206/112 and 224/134 and he showed a pulsus alternans. The lungs showed wheezing bronchitic râles and a few subcrepitant râles scattered diffusely.

The electrocardiogram showed right bundle-branch block (Fig. 1).

Summary.—Angina pectoris; right bundle-branch block; hypertension; pulsus alternans; attacks of cardiac asthma.

CASE 11.—Mrs. A. T., aged sixty-eight years, suffered from diabetes for several years and attacks of asthma usually worse at night. In these she would suddenly awake and sit up unable to breathe. She had pain in the left shoulder and left arm for four months.

Physical examination showed a moderate arcus senilis. The heart was enlarged and its sounds good. There were no murmurs or accentuations. The blood pressure was 222/98. The lungs showed wheezing which increased promptly after exertion. The urine contained albumin, sugar, and hyaline and granular casts. The vital capacity was much below the normal. The patient improved markedly under vasodilator treatment.

The electrocardiogram showed left ventricular preponderance and inversion of the T-wave in Lead I.

Summary.—Hypertension; diabetes; chronic nephritis; cardiac asthma.

CASE 12.—Mrs. B. M., eighty-three years old, had an attack of angina pectoris eight years before with terrific pain in the chest, radiating down the left arm. She had dyspnea, palpitation and constricting pain across the sternum which always re-

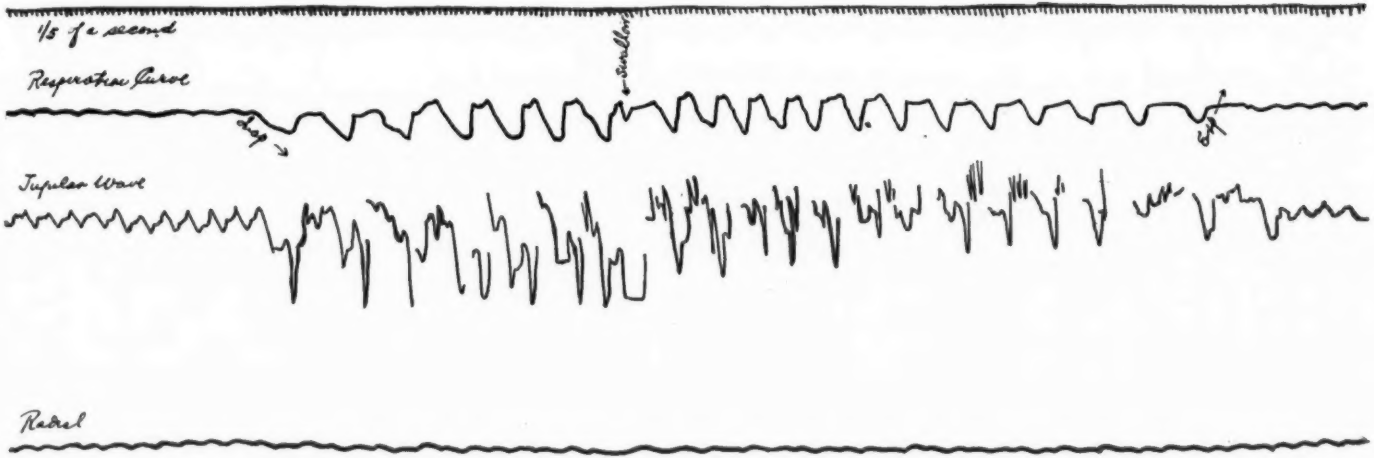


Fig. 2.—Cheyne-Stokes breathing in cardiac asthma (Case 9) showing pulsus alternans.

curred after walking one block. One year before she had had a severe anginal attack in which she became unconscious for a few minutes, and had some contortions of the face. An attack of unconsciousness recurred without pain. In one attack, there was dyspnea, gurgling and wheezing in the chest, ghastly pallor, cold sweat, and finally gasping for breath, and the coughing up of a little blood. This lasted two hours and returned at intervals of several weeks.

The heart was much enlarged to the left, the aorta not widened to percussion. There was a rough systolic blow at the apex and at the pulmonic area. The blood pressure was 212/106, with slight pulsus alternans. The vessels were tortuous peripherally and in the fundus oculi; there was marked arcus senilis. There was slight pretibial edema.

Summary.—Attacks of angina pectoris; aortitis; arteriosclerosis; hypertension; pulsus alternans; repeated attacks of cardiac asthma.

CASE 13.—Mrs. L. F., aged fifty-eight years, had dyspnea with continuous wheezing; especially in attacks during the night. These lasted several minutes with extreme panting for breath, cold sweat, and aching pain over the sternum and right half of the dorsal region which was relieved by nitrites.

The heart was enlarged and the aorta dilated. The first sound was very faint although the apex impulse was visible and the aortic second sound was accentuated. The lungs showed wheezing râles and congestion of both lower lobes. There was also slight pretibial edema. The blood pressure varied from 176/94 to 194/78. Pulsus alternans was always marked.

The electrocardiogram showed persistent right bundle-branch block with widening of the QRS wave and, at times, sinus arrhythmia.

Summary.—Attacks of cardiac asthma, with aching pain over the sternum and cold sweat; hypertension; chronic myocarditis; bundle-branch block; pulsus alternans.

SUMMARY

There are therefore basically two different forms of cardiac dyspnea. One depends upon the stasis in the pulmonary circulation associated with right ventricular deficiency for which I suggest the name "pulmonary asthma." It also develops in the late stages of left ventricular failure. The other depends on deficiency of the left ventricle alone; with irritability of the respiratory center producing reflexly attacks of paroxysmal dyspnea.

A useful clinical classification is presented of the various forms of dyspnea in the course of heart disease, based upon the physiological mechanism of dyspnea.

Pulmonary asthma is distinguished from paroxysmal cardiac dyspnea or cardiac asthma.

The organic conditions underlying pulmonary asthma are the marked valvular defects that develop with increasing heart failure in the course of chronic myocardial disease or chronic valvular disease. These attacks are characterized by their onset after strain, with both inspiratory and expiratory dyspnea, wheezing, congestion at the bases of the lungs, and cyanosis. The vital capacity, already below normal, is further diminished by stasis in the pulmonary capillaries. The condition may progress to pulmonary edema.

The main conditions in which paroxysmal cardiac dyspnea occurs are the aortic lesions and coronary artery disease; usually in elderly people. The attacks occur suddenly, commonly at night, with marked pallor, cold sweat and a feeling of anxiety or a suffocating oppression in the chest. The patient may jump out of bed, gasping for breath. They resemble attacks of coronary thrombosis. The dyspnea, marked pallor and the tracheobronchial wheezing are explained by stimulation of the respiratory, vasomotor, and vagal centers in the brain by anoxemia due to insufficiency of the propulsive force of the left ventricle (Wassermann). These attacks are relieved by morphine, which depresses the respiratory center, or by nitrites which improve its circulation.

Pulmonary asthma and paroxysmal cardiac dyspnea frequently coexist during the advanced stages of myocardial degeneration.

Cases are presented, illustrating both forms of cardiac dyspnea, with a statement of their differential diagnosis from bronchial asthma.

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Department of Clinical Reports

COMPLETE CLINICAL RECOVERY AFTER THROMBOSIS OF A CORONARY BRANCH*

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THIS case seems worth reporting for three reasons: first, because after having had a thrombosis of a branch of a coronary artery the patient has so fully recovered as to feel perfectly normal at present; second, because the clinical examination of this heart at present reveals only the most insignificant deviation from normal, unless the electrocardiogram or x-ray is used, and, third, because of the remarkable form of the electrocardiogram immediately after the attack and the character of the subsequent changes in the waves.

In January, 1924, he was in good health and going about his business which was that of a dry goods commission salesman. He had for many years considered that his wind was not good and had felt palpitation at times but had never considered himself sick. In 1917 a doctor had told him he had a nicotine heart. He was Jewish, thirty-eight years old, and appeared somewhat older than his age. He was a high strung, energetic, very active type of man, had never had any serious illness and denied syphilis.

On January 24, while on the way to business, he was attacked by a severe, heavy, constricting pain over the lower chest and upper abdomen radiating to the left shoulder and arm. He felt faint and short of breath and vomited. He was seen by Dr. Morris Zucker, who found him pale and apparently in shock, with the pulse weak and only 20 per minute. The pain continued for twenty-four hours, abating slowly. He continued to feel short of breath and vomited several times. He entered the New York Hospital on the service of W. R. Williams thirty hours after the attack. His temperature was 102°, pulse 100; respirations 28. The blood pressure was 90 mm. systolic, 70 diastolic. The leucocytes numbered 22,400, polymorphonuclears 82 per cent, small lymphocytes 13 per cent, large lymphocytes 5 per cent. The urine was normal and the Wassermann reaction negative. The heart was not enlarged, the sounds were normal, there were no murmurs. The lungs were clear of râles.

He continued to have some pain, especially on breathing, until forty-eight hours after the attack. The temperature varied between 101.8° and 103.8° on January 26, gradually fell to normal by January 31, and remained there. The pulse and respiration followed the temperature. On January 31 the leucocytes were 8,400, polymorphonuclears 71 per cent.

On February 3, he again had pain across the lower chest, radiating to the back and shoulders. On this day a pericardial rub was heard. After this he continued to do well and continued free of pain. He gradually gained in strength so that he was able to go home on February 14.

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His electrocardiogram, taken on January 28, four days after the attack, is seen in Fig. 1, record A. It shows normal auricular waves and normal A-V conduction time. The ventricular waves are strikingly unusual. The QRS group is abnormally prolonged, lasting for 0.14 seconds in Lead II. The R-wave is notched in all three leads and right predominance is suggested by the large S in Lead I with R smaller than S in this lead. The T-wave shows an abnormal form in Leads I and II having a position of 2 mm. above the isoelectric level in both of these leads and having a slight downward deflection in Lead II. This ventricular complex indicates interference with the spreading of the contraction wave and with the development of the contraction of the ventricles. The origin of the T-wave from a point upon the QRS group at some distance from the zero level is a feature which has been found commonly in records taken directly after a thrombosis of a branch of a coronary artery.[1]

During the following days the record changed slowly. Record B, taken on February 1, shows a slight change both in QRS and in T; while record C taken on February 4, shows no further change in QRS but the T-wave is developing a downward peak in both Leads I and II with a well developed upward convexity in Lead II before the downward peak of T. This is the feature of the T-wave which is so common when a coronary thrombosis is healing, or with marked narrowing of one coronary branch.[2]

Record D taken on February 8 shows a well developed downward T-wave in both Leads I and II, with a less definite upward convexity in Lead II. Record E taken on April 8, 1924, shows an increase in the voltage of the QRS group but the T-wave is little changed. A record taken January 3, 1925, is practically identical with record F which was taken July 7, 1926. The QRS group is practically the same but the T-wave shows a lessened voltage.

After his return home on February 14, he continued to gain strength. He was told to take theobromine sodium salicylate, 7½ grains three times daily, for one month periods, with rest intervals of seven to ten days. When seen on February 29 he said that he had no shortness of breath on walking 600 feet at an ordinary rate or on climbing one flight of stairs. He had had no pain of any sort. The heart was normal to ordinary clinical examination, the beats 84 per minute and regular. The waves of the electrocardiogram were practically identical with those of record D.

He continued thus until the middle of March, when he was wakened at night by a severe attack of pain across the shoulders especially severe around the right scapula. There was no pain in the anterior chest, no palpitation, dyspnea or prostration. (This may have been an attack of pulmonary embolism.)

I did not see him until three weeks later. At this time he said that since the attack he had been troubled with shortness of breath on climbing one flight of stairs, and on walking six blocks he would have to stop because of a pain in the region of the right scapula. For the last week he had, from time to time, felt a sense of a lump in the region of the apex beat. I found the heart not enlarged; the sounds normal; the blood pressure 98/74; the heart rate 66 per minute and irregular from many premature beats which the electrocardiogram proved to be both nodal and ventricular in origin.

Nitroglycerine did not relieve this scapular pain but he felt well otherwise and continued to take diuretin. The premature beats diminished in frequency as did also the "lump" feeling at the apex beat. The pain in the back gradually became less and disappeared.

He was next seen January 21, 1925. There had been no more attacks and for a long time no sign of the pain in the right shoulder and arm. He had no pain on

[1]Pardee, H. E. B.: Clinical Aspects of the Electrocardiogram, New York, 1924, Hoeber. Pardee, H. E. B.: An Electrocardiographic Sign of Coronary Artery Obstruction, Arch Int. Med., 1920, xxvi, 244.

[2]Pardee, H. E. B.: Heart Disease and Abnormal Electrocardiograms with Special Reference to the Coronary T-Wave. Am. Jour. Med. Sc., 1925, clxix, 270.

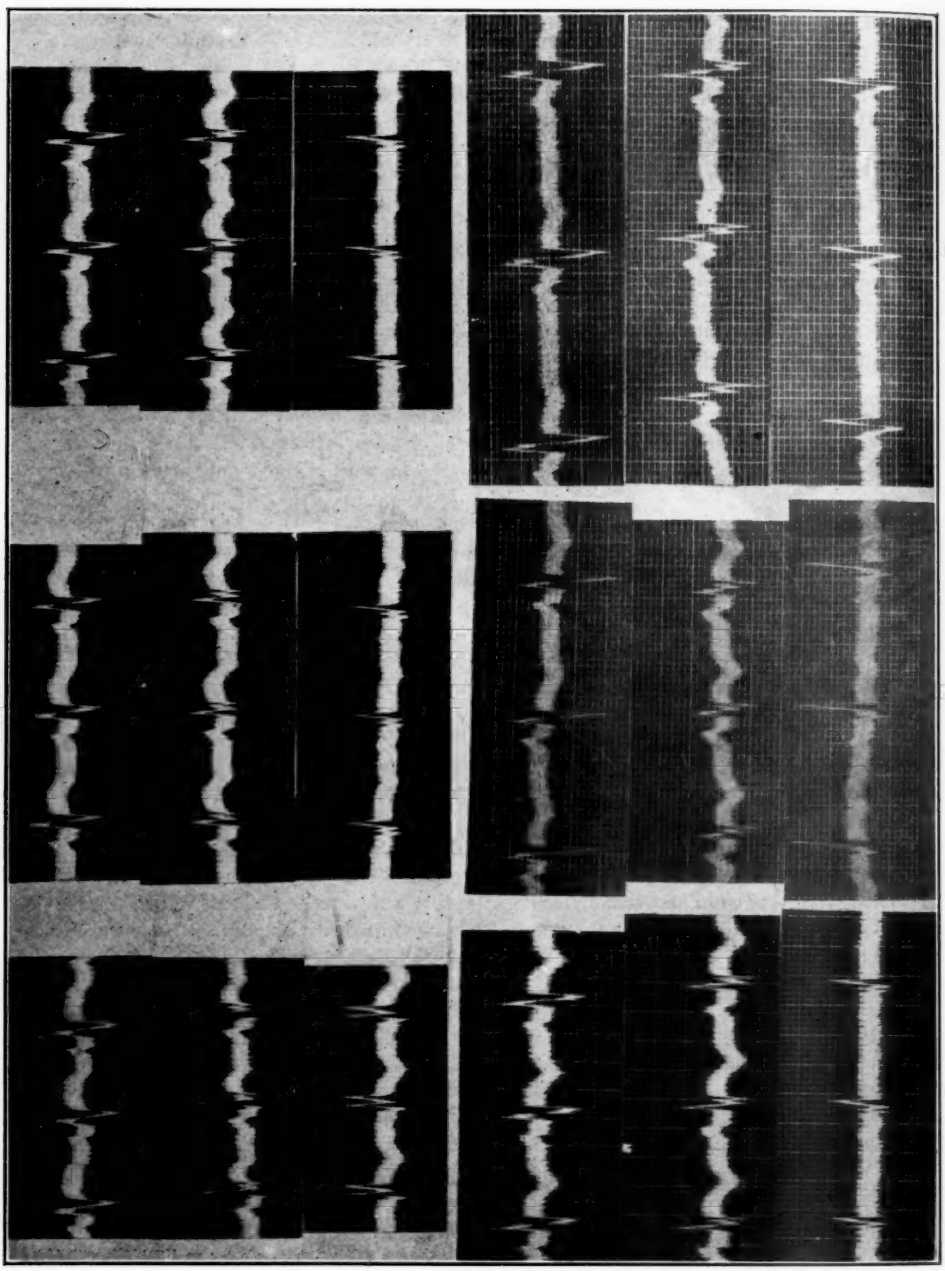

Fig. 1.—Six records to show the changes in the electrocardiogram from January, 1924 to March, 1927.

walking and no especial shortness of breath. He could climb two flights of steps and walk fast for from six to ten blocks (which is as far as he ever walks) before feeling short of breath. He said he believed he was as well now as before the attack except that now he noticed how he felt, while previously he did not.

While sitting talking to me he several times drew deep breaths, saying that it was

because he felt short of breath and that the deep breath relieved the feeling. This symptom I believe always to have a neurotic basis.

The examination showed the heart normal in size. The first sound at the apex was somewhat prolonged. The second sounds at the aortic and pulmonary area were normal. There were no murmurs. The heart rate was 66; rhythm, regular; blood pressure, 108/68. A test exercise, swinging 10 pounds 10 times from near the floor to over his head, produced no unusual dyspnea and only slight heart acceleration—a normal reaction to this moderate exercise. The electrocardiogram taken at this time was practically identical with record *F*.

He was next seen in July, 1926. There had been no pain in the left shoulder for several months. He considered himself quite well. He could walk a mile, but a short run made him feel afraid and made him short of breath. The clinical signs were unchanged, and the electrocardiogram is seen in record *F* of Fig. 1. An orthodiagraphic tracing of the heart (Fig. 2) showed a bulging of the right auricular and left ventricular margins, and the transverse diameter was definitely, though

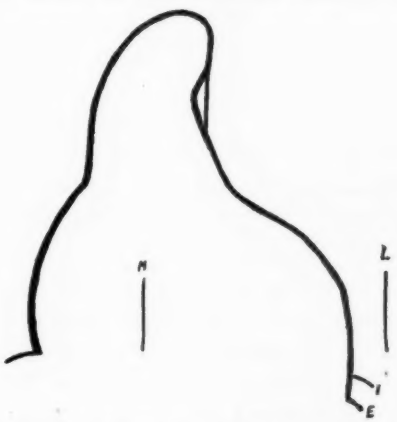

Fig. 2.—Orthodiagraphic tracing made July, 1926. *M.* Midline. *L.* Left chest wall. *I.* Inspiratory position of diaphragm. *E.* Expiratory position of diaphragm.

slightly, larger than the normal standard of half the chest diameter; this in spite of the fact that percussion and palpation did not show cardiac enlargement. The outline of the aorta was not dilated. It was even smaller than would be expected for one of his size.

He was seen again in March, 1927, and reported that he continued well and able to work as a taxi chauffeur. Examination shows no changes since July, 1926.

This man undoubtedly had a thrombosis of a coronary branch in January, 1924. The clinical history is typical and the electrocardiogram furnished additional proof of a definite lesion of the heart muscle. It is interesting that after this lesion he has been able to make a recovery to so nearly a normal state. It is particularly interesting that he shows neither precordial pain on exertion nor unusual shortness of breath, as these are the symptoms by which myocardial damage of this type usually makes itself known. We should expect that one with so definite a lesion would show one or both of these signs of coronary atheroma.

MENINGITIS COMPLICATING SUBACUTE BACTERIAL ENDOCARDITIS—WITH REPORT OF A CASE*

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THE literature of subacute bacterial endocarditis, under that title or some of its well-recognized synonyms, is gaining in annual volume and importance as the disease itself is becoming more widely understood and studied. However, in the many published reviews of cases rare mention is found of instances in which meningitis is a complicating feature.

Steinert[1] in 1910 in a discussion of acute and chronic streptococcus sepsis and their relation to articular rheumatism mentioned two instances of serious cerebral complications. The first of these two proved to be a case of pachymeningitis hemorrhagica interna as proved at autopsy. The other case developed the important meningitic symptoms of stupor, headache, vomiting and stiff neck, and the cerebrospinal fluid was under increased pressure upon puncture, with an increase in both polymorphonuclear leucocytes and lymphocytes. These phenomena disappeared spontaneously, and when the patient died a few weeks later the brain and meninges revealed no discoverable pathological changes to which a clinical symptom might have been attributed.

In 1915 Oille, Graham and Detweiler[2] in a discussion of streptococcus bacteremia in endocarditis recorded the case of a young woman with the complaint of severe pain in the lumbar region, who developed meningitis while under observation. The usual clinical signs of meningitis were absent but they obtained a turbid cerebrospinal fluid with increased number of polymorphonuclear, lymphocytic and epitheloid cells. A smear showed the presence of a gram-positive diplococcus. Owing to the lack of the conventional signs of meningitis the condition was considered focal and possibly of embolic origin. Blood cultures were positive for Streptococcus viridans and the patient was discharged from the hospital four months later in presumable health.

Libman[3] in 1918 referred to cases in which subarachnoid and intracerebral hemorrhages simulate meningitis clinically and in which the spinal puncture produces first a bloody fluid with later an increase in lymphocytes.

Blumer[4] in 1923, reviewing the assigned causes of death in 193 cases of subacute bacterial endocarditis, mentions two instances in which meningitis played the part of a terminal infection.

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Waldman and Kahn[5] have recently reported a case with mycotic aneurysm and meningeal symptoms. These latter consisted of an increasing neck rigidity and a positive Kernig sign. A spinal puncture was not done.

While there may be similar reports which have escaped our attention we have seen references to these few cases only. The following case report is offered as an additional example of this unusual combination of clinical findings and also because it serves to present certain interesting features in the way of differential diagnosis.

CASE No. 55433, O. E., a white man, aged thirty-six years, was admitted to the In-patient Department of the Henry Ford Hospital on Feb. 6, 1925, with the complaint of general weakness. He was American born, a glazier by trade, and had been married for twelve years, the father of four children. Wife and offspring were living, and in an apparent good state of health. There was no history of acute rheumatic fever, chorea, scarlatina, diphtheria, typhoid or acute tonsillitis. He had had rather marked oral sepsis, and admitted a probable chancre sixteen years previously. He had had no intensive antiluetic therapy.

His present illness dated back five months to August, 1924, when he developed arthritis in the right hip. His physician administered some intramuscular medication—nature not known to the patient—the reaction from which incapacitated him for four days. Upon the fifth day he was able to return to the physician's office where he was prevailed upon to receive a second injection, after which he was practically confined to the house for weeks. An x-ray examination of the hip at that time was negative and a blood Wassermann was reported as two-plus.

The patient took a several weeks' rest at a relative's home in a small village but failed to regain completely his strength or appetite. During this period all upper teeth were removed, some of which he stated were "rather bad." About November he began to experience severe occipital headaches, with photophobia and some dizziness associated with chills and fever. These would confine him to bed for perhaps a fortnight, and would recur within a few days after attempting to regain his feet. These recurrent headaches persisted until time of admission, although he was admitted during a free interval. There has been marked loss of strength, weight and appetite. A rather obstinate constipation has been controlled with difficulty.

Upon admission the patient appeared to have been the object of a severe chronic illness. There was a definite pallor and marked emaciation. He was feeble and seemed barely able to walk to his room. There was a general lymphadenopathy in which the cervical, axillary, epitrochlear, inguinals, and parasacral (rectal examination) were definitely palpable, discrete, rather hard, and in a few instances, slightly tender. The peripheral vessels were definitely thickened and the heart showed the classical signs of an aortic insufficiency, with, however, only moderate cardiac enlargement. The pulse was regular and Corrigan in type. A "pistol shot sound" was heard over the femoral artery. Blood pressure readings showed a systolic pressure of 100 and a diastolic pressure of 40. The fingers showed slight curving of the nails. A scar was present on the corona penis. Ophthalmoscopic examination showed evidence of a moderate degree of optic neuritis and moderate arteriosclerosis.

From the history and physical findings the first observer felt that the entire clinical picture could be explained upon the basis of a generalized syphilitic involvement. Upon admission the blood count showed R. B. C. 3,800,000, hemoglobin 62 per cent, and W. B. C. 8,500. Urine: Albumin 3-plus, with hyalin and granular casts. The following day the temperature became elevated to 100° F. and the patient com-

plained of a most severe occipital headache, stiff neck, and photophobia. There was a positive Brudzinski neck sign and an equivocal Kernig sign at this time.

With a tentative diagnosis of syphilitic meningitis a spinal puncture was done and the fluid was found to be under increased pressure, 28 mm. of mercury; 25 c.c. of ground glass-like fluid was withdrawn, which showed a cell count of 2,400 cells per c.mm. of which 94 per cent was polymorphonuclear leucocytes.

In spite of a negative result from the examination of smears for organisms and of twenty-four-hour cultures, it was felt that the possibility of a meningococcus meningitis was by no means ruled out, and the succeeding day 28 c.c. of an antimeningococcus serum was administered after withdrawal of 30 c.c. of fluid, which was again under increased pressure. Three similar administrations of such serum were made during the next ten days in decreasing amounts, with the result that the spinal fluid became crystal clear and the cell count dropped with each succeeding treatment until it reached only 45 cells per c.mm. At each subdural drainage the patient professed marked relief from his headache.

It was felt that the comparatively mild symptomatology was incompatible with the original spinal fluid findings of a syphilitic basis, and further doubt was thrown upon this original diagnosis by a negative blood and spinal fluid Wassermann reaction. Repeated cultures of the spinal fluid continued negative for other organisms as well as the meningococcus. A more exhaustive search was carried out for the cause of the spinal fluid leucocytosis. Tenderness on pressure over the spinous process of the third cervical vertebra suggested caries of that bone with discharge into the subdural space. X-ray films of this region revealed no pathological conditions.

The suggestion of the presence of a subacute bacterial endocarditis was advanced, with possible meningeal metastatic embolism. Blood cultures were repeatedly positive for Streptococcus viridans. The low-grade fever continued somewhat intermittently and a few petechial hemorrhages were observed in the skin of the upper extremities and one such hemorrhage in the retina, while urinalysis revealed a few red blood cells occasionally.

With the presence of this type of an infection established, specific therapy was attempted in the form of intravenous administration of gentian violet. Four injections of 4 mg. per kilogram of body weight were given on alternate days in 1 to 500 solution.

During his stay in the hospital the red blood corpuscles dropped to 3,200,000 and the hemoglobin to 60 per cent. There was a constant albuminuria of three- to four-plus, with many casts, hyalin and granular. The phenolsulphonephthalein test was returned 58 per cent upon one occasion and 48 per cent upon another. There was no nitrogen retention.

The patient was then discharged upon a regime of general tonic and highly nutritious food, with complete rest. He was again admitted four weeks later for forty-eight-hour observation, having gained eleven pounds in weight and some strength. At this time the cerebrospinal fluid was clear, with a count of twenty-six cells and the Streptococcus viridans was recovered by culture. The blood culture was again productive of the same organism.

A few weeks later he suffered a hemiplegia, and showed further petechiae. From this time on he gradually failed, exhibiting increasing cachexia and anemia, and died at his home on June 5, 1925, approximately ten months after the onset of his illness.

COMMENT

This additional case of meningitis complicating subacute bacterial endocarditis is similar in several respects to those reported by Steinert and Oille, Graham and Detweiler, although the latter was not claimed to conform to the classical diagnosis of this form of endocarditis. Like

both these cases, however, the symptoms and spinal fluid findings cleared. In accord with the latter authors we attributed the circumstance to an embolic manifestation. The administration of antimeningococcus serum was not made because any observer was convinced of the existence of a meningococcus infection but as a measure of safety first. The clearing up of the symptoms and spinal fluid findings in this case would probably have taken place spontaneously, in the light of the experience in the cases quoted, and was probably aided as much by the repeated drainages as by the administered serum, although the latter may have had some nonspecific effect upon the meninges.

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AURICULAR FLUTTER WITH ESTABLISHED COMPLETE HEART-BLOCK*

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SINCE the introduction of electrocardiography, the recognition of auricular flutter has become common. The production of complete heart-block by the administration of large doses of digitalis during the treatment of auricular flutter likewise occurs, but established complete heart-block with auricular flutter is a rare and unique association of abnormalities. The first observation of this nature was made by Jolly and Ritchie[1] in 1910. Another case has been reported by de Boer.[2] The following is the only case that has been observed at the Mayo Clinic in 168 cases of auricular flutter.

A man, aged fifty years, consulted us because of shortness of breath on exertion, and slow pulse of about five years' duration. A mother and one older sister had died from apoplexy. The patient did not give a history of significant illnesses. He had had the usual diseases of childhood, and tonsillitis at the age of forty. He was a man of temperate habits. A physician had been consulted, who found the pulse to be very slow, 32. The patient was placed at rest in bed for several weeks and did not attempt work for eighteen months. He was much less dyspneic at the end of this time but the pulse rate remained constantly slow. Since his resumption of work, the shortness of breath has increased, but is always more marked when he sits or lies down. During the last year he has slept poorly, owing to difficulty in breathing.

*From the Section on Cardiology, Mayo Clinic.

There have been no syncopal attacks. During the last three or four months he has been aware of a peculiar sensation in the chest which he described as a fluttering, although he is positive that the pulse rate has been constantly slow. There were no other noteworthy complaints other than periodic migraine headaches which had been abating during the last five years.

Examinations.—The patient was 5 feet, 7 inches tall and definitely overweight, weighing 173 pounds. Cardiac dullness extended 4.0 cm. to the right and 15.0 cm. to the left of the midsternal line. There was no arrhythmia, and no murmur. The heart tones were of fairly good quality and the rhythm was remarkably slow (36

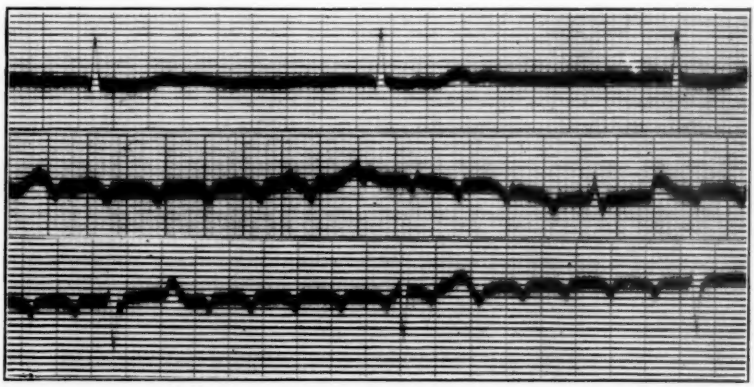

Fig. 1.—Record obtained Feb. 15, 1926. Auricular flutter and complete heart-block. Ventricular rate, 36, auricular rate 236. Left ventricular preponderance.

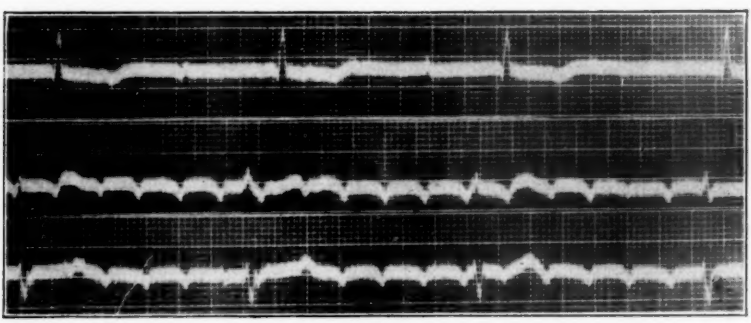

Fig. 2.—Record obtained Feb. 22. Ventricular rate 43, auricular rate 225.

beats each minute). Inspection of the jugular bulbs revealed extremely rapid and apparently regular venous pulsations. There was no edema. A moderate degree of peripheral arteriosclerosis was present. A slight impulse on coughing was elicited over the right inguinal ring.

The systolic blood pressure varied from 150 to 160 mm. and the diastolic from 94 to 100. Repeated examination of the urine occasionally disclosed faint traces of albumin and a few leucocytes. The Wassermann reaction on the blood was negative. The hemoglobin was 75 per cent (Dare) and the leucocytes numbered 8,600. There was 30 mg. of urea for each 100 c.c. of blood. The phenolsulphonephthalein test revealed an excretion of 50 per cent of the dye. Roentgenograms of the chest showed moderate enlargement of the heart, and the initial electrocardiogram auricular flutter

with complete heart-block. The ventricular rate was 36 and the auricular rate 236. Complete auriculoventricular dissociation existed.

Myocardial degeneration of the arteriosclerotic type with auricular flutter and complete heart-block was diagnosed. In view of the moderate elevation of the blood pressure, it is possible that a greater degree of hypertension had existed.

An attempt was made to abolish the flutter without results. It was deemed inadvisable to administer digitalis owing to the complete heart-block, and the administration of quinidin had no apparent effect.

The patient is moderately active, but is still complaining.

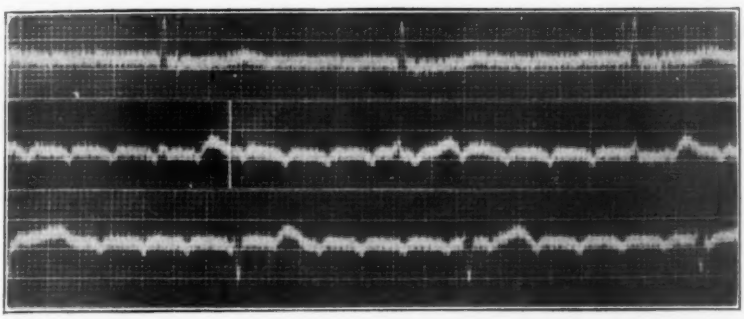

Fig. 3.—Record obtained March 5. Ventricular rate 40, auricular rate 214.

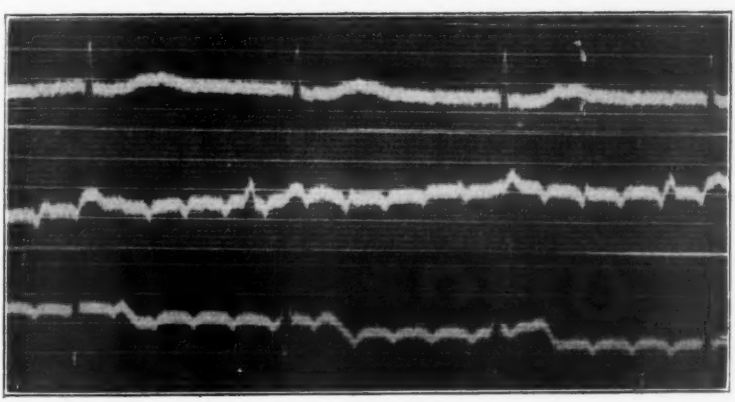

Fig. 4.—Record obtained March 12. Ventricular rate 46, auricular rate 250.

DISCUSSION OF ELECTROCARDIOGRAM

The first electrocardiogram obtained February 15, 1926 (Fig. 1), revealed auricular flutter and complete heart-block. Complete auriculoventricular dissociation was apparent. The ventricular rate was 36 and the auricular rate 236. There was preponderance of the left ventricle. The ventricular complexes were normal except in Lead II where alternate complexes were apparently submerged. This phenomenon is constant in all the records. Virtually, daily tracings were obtained which are too numerous to reproduce. February 22 (Fig. 2), the ventricular rate was 43 and the auricular rate 225. The succeeding records are similar (Figs. 3 and 4).

COMMENT

The rarity of auricular flutter with established complete heart-block justifies this report. It is novel in my experience, being the only case among 168 of auricular flutter occurring in the routine electrocardiographic examinations of 40,000 patients.

As nearly as can be determined, the establishment of complete heart-block preceded the development of flutter. The patient was positive that his pulse rate was remarkably slow during the entire five-year period. Three or four months prior to his visit to the clinic, he became aware of a peculiar sense of fluttering in the chest, although the pulse rate remained slow. It is probable that the appearance of this symptom marked the onset of flutter. This, however, cannot be positively stated as the tracings made in the clinic were the first to be obtained.

The long and continuous history of unusually slow pulse in conjunction with the subsequent electrocardiographic records justifies the conclusion that complete heart-block is an established mechanism and one presumably resulting from anatomic changes interrupting the transmission of impulses through the bundle of His. The rapid visible venous pulsations of the jugular bulbs indicated the presence of flutter before electrocardiograms were obtained.

It is of interest that the patient is able to be reasonably active with such marked disturbance of cardiac action.

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Department of Reviews and Abstracts

Collective Review

GALLOP RHYTHM

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INTRODUCTION

ALTHOUGH one ordinarily thinks of two heart sounds, the presence of a third, or gallop sound, is by no means uncommon. The third sound may be so faint as to be detected only after careful search, or it may be louder and clearer than either of the other sounds, but in any case it is distinct and separate. It occurs during diastole and changes the rhythm for each heart cycle from 2:4 to 3:4, thus suggesting the sound of a galloping horse. The presence of a third sound, or gallop rhythm, has offered an interesting field for study and speculation, and in spite of much work, the subject presents many unsolved problems. In view of the clinical and theoretical importance of gallop rhythm, it has seemed worth while to review some of the more important phases of the subject. Even a brief review must touch upon the early descriptions and the definition of terms, the theories of the causal mechanism together with the experimental evidence advanced in support of such theories, the frequency of occurrence in health and in disease, and the clinical and pathological significance. Such a review is necessarily fragmentary and can do little more than indicate the high spots already reached and the paths leading toward a clearer understanding of the subject.

HISTORICAL OUTLINE

The term "bruit de galop" was first used by Bouillaud[86] in 1847, and a few years later the term "galop rhythmus" was introduced by Traube.[41] Each of these men used a descriptive term for teaching purposes to describe a rhythm which, although already recognized, was very little understood. Reduplication of one or both heart sounds was discussed by Bouillaud[15] in 1835 but apparently the first clear description of a gallop is that of Charcelay[23] of Tours, who in 1838 reported a case in which a typical presystolic gallop was present for some days. Charcelay remarked that the presence of a third heart

sound was a singular and very rare anomaly, and although he did not use the term gallop, he described the signs accurately, reported the postmortem findings, and advanced the theory that the phenomenon was due to the audible contraction of an hypertrophied auricle. Other early mentions of accessory heart sounds were made by Gendrin in 1842,[45] by Bouillaud in 1853,[14] by Skoda in 1854,[103] by Stokes in 1855,[105] by Potain in 1856,[83] and by Duroziez[32] in 1862. In 1855 Drasche[31] remarked that reduplications were much more common than one would suspect from the literature and that they might be due to asynchronism, to double contraction, to sudden tension, or to other causes. Moreover he emphasized the need for further work on the subject, thus establishing a precedent to be followed by practically everyone who has given the subject any notice whatsoever.

In the early descriptions there is a confusion of terms and it remained for Bouillaud's disciple, Potain, to bring order by defining the terms used to describe gallop and accessory sounds in general. Potain[83-91] described the typical gallop so clearly that he is quoted in practically every review of the subject; he differentiated between gallop and split sounds; and he gave a clinical and theoretical discussion to which little can be added today. According to Potain, whose views are generally accepted, a reduplication or split sound is one of which the two parts are of the same quality and pitch, and are separated one from the other by a very short interval; while a gallop is characterized by the presence of a dull sound and shock added to the normal sounds, but separated from each by an appreciable interval. The added sound is usually short and dull, a sort of thud, often better felt than heard, and frequently missed entirely if one listens only with a stethoscope. It is usually detected in the region between the apex, the left border of the sternum, and the second rib, and is sometimes present over a very limited area. The third sound is always diastolic, and a gallop is classified as protodiastolic, mesodiastolic, or presystolic depending on the time at which the third sound occurs. The typical gallop is presystolic. The protodiastolic gallop is often described as the "bruit de rappel" or "diastolic echo,"[14] and is likened to the recall on a drum or the rebound of a hammer on an anvil. The third sound of the protodiastolic gallop is sometimes called the "opening click of the mitral valve," and is often classed as a distinct entity apart from gallop.

In England the term gallop was not adopted as early as on the continent, and we read of true and spurious reduplications. A spurious, simulated, or false reduplication is the "interpolation of an extra sound of doubtful mechanism following the second sound which may thus seem to be doubled."[82] The description is clear enough and the words, "of doubtful mechanism," seem particularly well chosen.

In the earlier literature a reduplication may mean a split sound, a

gallop, or almost any type of arrhythmia. Charcelay[23] described as reduplication of both sounds of the heart, what was apparently a case of coupled beats. In 1855 Austin Flint[40] described a similar case in which the rate was 160 at the apex and 80 at the wrist, and in 1881 Henry[51] described a third case of the same sort. This was considered reduplication of both sounds of the heart, due to alternating contraction of the right and left ventricles. Henry showed cardiograms from his case and the tracings are characteristic of early premature beats occurring regularly. The weak, early beat which failed to open the semilunar valves was believed to be due to the isolated contraction of the right ventricle.

Attempts have been made to classify gallops according to the accent as dactyl or anapest.[79] Such distinctions are without significance, for it has been shown that the accent may fall on any one of the three beats (—′ ∪ ∪, ∪ —′ ∪, or ∪ ∪ —′). The attempt to classify the gallop as the ordinary, hunting,[41] or school gait seems rather futile in a motor age when men think in terms of gears.

Potain classified gallops as right or left according to the side of the heart in which he believed the extra sound to originate. A typical left-sided gallop occurs in cases of hypertension with beginning cardiac failure and is common, while a right-sided gallop is unusual[5-8, 28-30] and occurs with cases of hepatic or gastrointestinal disturbance. The distinguishing feature of a right-sided gallop seems to be that the third sound is heard near the tip of the sternum instead of farther to the left. Owing to the possibility of changes in the position of the heart or in the relative position of the chambers, this point seems unimportant. It has been said that the usual gallop is in all probability produced in both sides of the heart,[80] and until we know more of the mechanism of gallop, it seems unsafe to state that the right-sided form can be distinguished from the left.

The so-called systolic gallop has been observed in France, and although noted by some,[1, 27, 57, 65] it has been questioned by others. When present it occurs in the course of typhoid fever or other acute infections, usually shortly before a fatal termination. The extra sound follows the first sound and resembles a prolonged sound or murmur; the second sound is clear. The extra sound varies from time to time but is not influenced by respiration. It is always associated with a dicrotic pulse and is believed to depend on low tension and poor heart tone, with perhaps a double systolic effort. It has not been studied graphically, but Michaud and Fleisch[72] noted the presence of one or two vibrations between the first and second sounds in records of the heart sounds from one of their patients. The nature of this sound is quite unknown, and in any case it differs fundamentally from a true gallop in which the third sound is always diastolic.

Under the general heading of "rhythm à trois temps" Bard[4] has

attempted to classify all accessory heart sounds as "dédoublements" due to asynchronism between the right and left sides of the heart; "rédoublements" or repetitions of a sound; "dissociations" caused by the dissociation of the various elements of a sound; and "bruits accessoires" which may be due to audible auricular contractions, to sudden distention of the ventricle, or to the opening snap of the mitral valve. To be useful this classification must be supplemented by a clue for determining how the various split or added sounds are produced. It is easier to recognize a "rhythm à trois temps" than to understand its mechanism.

MECHANISM OR CAUSE

One of the earliest and most popular theories advanced to explain gallop rhythm was that of asynchronism of the right and left sides of the heart—of the actual contraction as well as of the closure of corresponding sets of valves. It was believed that the contraction of the ventricles and the closure of the corresponding sets of valves were synchronous under normal conditions, but that in disease, owing to such factors as differences in pressure in the pulmonary and systemic circulations, the two sides of the heart might act independently, causing a true hemisystole. All degrees of asynchronism were considered possible, even the complete hemisystole assumed by Charcelay, Flint, and Henry to be the simplest explanation of a pulse deficit due to premature beats. The belief in asynchronism rested on such theoretical explanations, on observations that in the dying heart irritability[100] of the right heart persisted longer than that of the left, and on a few reports of seeing asynchronous contraction of the hearts of laboratory animals.[9] The theory has been abandoned bit by bit, for it seems not only unsound physiologically, but impossible anatomically. Mackenzie[71] said rather cautiously that asynchonism was rarely if ever found except in the dying heart, and all experimental work has indicated that asynchronous contraction is not to be considered as a serious possibility. Still this is the theory brought forward to explain gallop, not only in most of the older textbooks,[110, 108, 21, 11, 12, 102] but in some of the more recent[74] ones as well. At one time the idea that gallop depended on asynchronism was so firmly established that those who doubted the possibility of asynchronous contraction felt forced to deny the possibility of reduplication of the first sound.[45, 92] If reduplication of the first sound depended on asynchronous contraction, and if that were impossible, there could be no reduplication.

The question was approached from a different angle by those clinicians who stated that quite apart from its possibility, asynchronism was an inadequate explanation of gallop rhythm. Walshe[110] found it difficult to understand why, if due to asynchronism, a gallop sound

was often audible only over a very limited area. In 1875 Exchaquet,[36] in a discussion of gallop rhythm based on the careful clinical study of forty cases, noted that when a gallop disappeared, the third sound became fainter and fainter, but that it never approached and blended with the first sound as it would do if caused by asynchronism. The next year Johnson[62, 63] advanced the following arguments against the asynchronism theory: When the first sound is reduplicated, that is, with a presystolic gallop, the second sound is single, so that one must assume differences not only in the time, but in the duration of the contraction of the two sides of the heart. Mechanically the idea is hard to grasp. The structure of the cardiac muscle makes the idea seem impossible. Asynchronous contraction is never observed in animals. The theory supposes a lag in the contraction[56] of one or the other ventricle depending on an increase in pressure in either the pulmonary or the systemic circulation, but it is always the presystolic sound which is abnormal and which disappears with a return to the two-tone rhythm. In other words, when a gallop disappears, the ventricle which contracts first, supposedly at the correct time, lags so as to become synchronous with its delayed partner. Finally the time of a presystolic gallop sound corresponds to that of the friction rub in cases of pericarditis involving the auricle, and it seems reasonable to attribute the presystolic sound to auricular systole. Although these objections were never satisfactorily answered, the theory of asynchronous contraction continued to have its adherents.

The theory of asynchronism as a cause for gallop must be abandoned, but it may not be out of place to say a few words concerning split sounds. There are many excellent descriptons of split or reduplicated sounds, and practically all observers agree that reduplication is common both in normal and in pathological conditions. A reduplication differs from a gallop in that the two parts of the sound have the same pitch and quality and are separated by a very short interval so that the 2:4 rhythm persists. Moreover, a shock is not a characteristic feature of reduplication. Reduplication of the first sound is most common at the apex, of the second at the base, and under normal conditions the reduplication seems to depend on the phase of respiration. Potain[84-88] believed that pathological splitting of the first sound was rare while that of the second was common and was due to differences in pressure. The frequency of a reduplicated second sound in cases of mitral stenosis has been noted since the time of Duroziez.[42, 56, etc.] Potain[86] taught that with slight stenosis the first part of the reduplicated sound was best heard at the aortic area; that with moderate stenosis there was no reduplication, but that the second sound was accentuated over the pulmonic area; and that with marked stenosis there was reduplication, with the first part of the second sound best heard over the pulmonic area. A contribution to

the subject was made in England[35, 93] when it was pointed out that the sound produced at the pulmonic valve was heard over a very limited area and was not transmitted, therefore that an early diastolic sound heard at the apex could not be due to delayed pulmonic closure.

Experimental studies have added to our understanding of split sounds. Graphic records[33, 38, 52, 68, 70, etc.] have shown how complex are the vibrations of the first sound and how easy for a delay in one of the elements to produce a prolonged or split sound—a dissociation, according to Bard's classification. Sachs[96] believes that splitting of the first sound is without significance. Castex[22] and Lewis[68] have found electrocardiographic evidence of bundle-branch block in cases with split sounds; other observers have failed to find this consistently, and Battaerd[10] reports normal heart sound records when the electrocardiogram showed evidence of bundle-branch block. It may that there is always a very slight difference in the time of contraction of the two ventricles.[2, 53] Katz,[62] who analyzed 4,137 simultaneous records of right and left ventricular cycles in animals, found that under normal experimental conditions neither the beginning nor the end of systolic ejection is simultaneous in the two ventricles. Vagus stimulation delays the end of contraction in the right heart; venous infusion prolongs and asphyxia shortens systole, in the right, in the left, or in both sides equally; compression of the aorta or of the pulmonary artery gives variable results. In any case, however, the degree of asynchronism is very slight. These experiments serve to differentiate all the more clearly between split sounds and a true gallop, and to show the fallacy of many of the theories advanced without experimental basis.

Other discarded theories are that gallop is a systolic event, and that it represents an active diastolic process. D'Espine[30] held that gallop rhythm could be explained on the basis of a polysystole, and Bouveret and Chabalier[16] believed that there might be a double systolic effort. Accurate timing has shown the fallacy of such theories, and it has been noted that they were based on an incorrect interpretation of tracings. D'Espine assumed a double contraction to explain the presence of two phases in the tracings of intraventricular pressure during systole; but H. Chauveau[25] showed that the first of these corresponded to the period of rising pressure before the opening of the semilunar valves and that the second was the period of systolic ejection, but that there was no interruption of contraction. Bouveret and Chabalier based their arguments on the presence of a double elevation of the cardiogram, a common finding, but one which does not necessarily imply a double contraction of the ventricle.[76, 80] The fundamental criticism of this theory is that it fails to recognize that gallop is a diastolic event. The same criticism applies to the suggestion

that gallop may be due to the dissociation of the muscular and valvular elements of the first sound.[3]

The theory of an active diastolic process is very attractive. The shock and, at times, the abrupt character of the gallop sound suggest activity. Brauer[18] believed that there was an active relaxation; A. Chauveau,[24] noting changes in intraventricular pressure during the period of intersystole, suggested active movement of the papillary muscles or at the aortic ring. Roy and Adami[95] studied the action of the papillary muscles, and found that it would be most unusual for any contraction of these structures to occur during diastole. Electrocardiographic evidence of the absence of electrical activity during diastole is usually taken for evidence of the absence of muscular activity at this time,[77] especially as there is no other evidence, either theoretical or experimental, to support the theory.[106]

In 1838 Charcelay[23] associated the third sound of a presystolic gallop with auricular systole. He did this because the sound was heard over the auricle, it corresponded in time to the auricular systole, and at autopsy the right auricle was found to be greatly hypertrophied. Later observers have agreed that the presystolic sound coincides in time with auricular systole, and two theories have been advanced to explain the relation between the two. One of these is that the sound is a muscle tone, due directly to the auricular contraction. It is well known that auricular sounds are heard under certain conditions,[61] and it has been demonstrated that strips of contracting heart muscle can produce sound even when all other possible factors are ruled out. One of the most curious reports of audible auricular contractions is that of Clark, Ellis, and Shaw,[26] published in 1858. A criminal was hanged at 10 A.M. At the end of fourteen minutes the heart sounds had ceased and at the end of one hour an autopsy was started. At 11:30 a pulsation was observed in the right subclavian vein, and a single heart sound was heard occurring 80 times to the minute. On opening the chest the right auricle was found to be contracting regularly, although the other chambers of the heart had ceased to beat. The contraction continued steadily for some time and irritability on stimulation persisted for several hours. It is well known that in some cases of heart block the auricular sounds may be audible, and graphic records of these sounds have been obtained in a number of cases. Two questions now arise: Why are the sounds present in some cases but not in all? How can audible auricular contraction produce a protodiastolic gallop?

In answer to the first question it has been said that auricular hypertrophy is a necessary factor in the production of the sound. In reports of postmortem findings from cases of gallop the presence and absence of auricular hypertrophy are noted with almost the same frequency. Moreover gallop appears during acute toxic conditions when

hypertrophy is out of the question, and even in cases where auricular hypertrophy is proved after death a gallop may be present one day and absent the next. Evidently some other factor is necessary and possibly this factor is prolonged conduction time. Some writers say that the auricle always produces a sound, but that when the conduction time is normal the sound merges with the first sound, and that the interval between the two can be detected only when the A-V conduction time is prolonged. Laubry and Mougeot[65] studied the conduction time in cases of gallop by means of simultaneous venous and cardiographic tracings and found that it was usually lengthened. More recent studies have been made by measuring the P-R interval of the electrocardiogram.[13, 47, 112] The results are variable and the most one can say is that in cases of gallop the conduction time is often, but not always, prolonged. No studies explain satisfactorily how an audible auricular contraction can produce a protodiastolic gallop when the gallop sound precedes the auricular systole.

The other theory is that, while auricular systole may be an indirect cause, the direct cause of the gallop sound is vibrations set up by a sudden rush of blood from auricle to ventricle. In order to understand this theory it is necessary to consider the relationship between gallop rhythm and the normal cardiac cycle. Potain observed that a gallop might be present at one time or another in 20 per cent of normal persons, and he as well as Barié,[6] Exchaquet,[36] H. Chauveau,[25] Müller,[73] Robinson,[94] and others emphasized the idea that a gallop is the exaggeration of a normal phenomenon, always present, but not usually observed. As long as gallop rhythm was believed due to asynchronism, to polysystole, or to active diastole, this view was necessarily disregarded. Laboratory work has supplemented clinical observation and has added to our understanding of normal and abnormal heart sounds and of the close relation between the two.

Earlier experimental work was done with cardiographs and, in animals, with cannulae and plethysmographs, and it was shown that in the cardiogram and in the volume and pressure curves there were waves corresponding in time to the gallop sound. An indication of these waves might be found in the absence of gallop, but when a gallop was present, the waves were usually exaggerated. In 1907 Gibson[46] in England and Hirschfelder[54] in this country called attention to the association between an early diastolic heart sound and a wave, *b* or *h*, between the *v* and *a* waves of the jugular tracing of normal individuals. In the same year Einthoven[33] noted the presence of early diastolic vibrations in one of his tracings of the heart sounds. He failed to find these vibrations associated with the wave in the venous pulse, but as he noted, his jugular tracing was not wholly satisfactory. More recently Thayer,[106, 107] Bridgeman,[19, 20] and Eyster[37] have tried to correlate the *h* wave and the third sound, and have

found that there is a common, but not constant, relation between the two; either may occur alone, but when both occur together, they coincide in time. Thayer pointed out that the *h* wave was certainly due to changes in the right side of the heart, while the third sound was probably due to changes in the left side, and, therefore, that it would not be necessary for the relation to be constant.

GALLOP AND THE THIRD HEART SOUND

A great revival of interest in the subject of gallop has followed Thayer's work on the third heart sound, published in 1908. Thayer found that an early diastolic sound was present in 65 per cent of healthy young persons and also in a number of dogs. In dogs he observed a third sound and shock associated with a sudden distention of the ventricle early in diastole. He studied the relation of the sound and shock to other events in the cardiac cycle and found that they coincided with a protodiastolic elevation of the apex cardiogram, with the *h* wave when this was present, and with the end of the rapid early diastolic filling. His findings suggested that early in diastole some structure was thrown into sufficient tension to produce audible vibrations and that at this time there was a temporary delay in the filling of the ventricles.

Bridgeman,[20] working in Thayer's laboratory, confirmed these findings and studied graphic records of the heart sounds taken simultaneously with other records. He found the third sound present in thirteen out of sixteen healthy boys. The second sound began 0.30 seconds after the onset of the first, and the third sound 0.45 to 0.48 seconds after the onset of the first or 0.13 to 0.18 seconds after the second. The pitch of all three was found to be between 33 and 50 vibrations to the second, and for two cases the relative insensities were calculated as 37:28:1 and 10:70:1. The time relations agree with those given by Lewis[68-70] and by Einthoven.[33] Eyster[37] has added several points of interest. The duration of the third sound varies from 0.02 to 0.1 seconds, with an average of 0.36, and does not increase with increase in the length of the cardiac cycle. The time between the second and third sounds is fairly constant but varies inversely with other features of the cardiac cycle, that is, it is shorter with a long cycle. After exercise the third sound occurs earlier and is of longer duration. The time between the third and the first sounds depends on the heart rate, for with an increased rate the greatest change is a shortening of the period of diastasis which brings the third and first sounds nearer together.

Bridgeman[19] noted that in eleven of his sixteen boys there was evidence of a presystolic sound, and similar evidence is found in records of Battaerd,[10] of Eyster,[37] and of Michaud and Fleisch.[72] According to Bridgeman this sound occurs 0.07 seconds before the

first sound or about 0.02 seconds after the onset of auricular systole. It causes electrical vibrations, with a wave showing displacement in one direction, indicating dampening at the source. The vibration frequency is about 25 per second, therefore is below the limits for human hearing. The duration of the sound is 0.04 seconds and its amplitude about one-eighth that of the first sound. It is increased by exercise, recumbent position, elevation of the limbs, and other measures which tend to bring out the early diastolic sound.

These observations make it clear that a protodiastolic sound, the third heart sound, and also a presystolic sound may be present in healthy young persons and also that both presystolic and protodiastolic sounds may be present at the same time. It remains to discuss the theories as to the cause of these normal sounds, the frequency of their occurrence, and their importance in understanding a pathological gallop.

Each sound is assumed to be due to vibrations set up by a sudden rush of blood from auricle to ventricle, the old theory on which Barié[7] explained gallop. To understand this theory it is important to understand diastole. Formerly it was taught that most of ventricular filling occurred during auricular systole, but Henderson showed that this was not so and that the ventricle filled early in diastole. Recently Wiggers and Katz[112] have found that anywhere from 18 to 60 per cent of ventricular filling may take place at the time of auricular systole. The three determining factors seem to be the time at which auricular systole occurs, the completeness with which the ventricle is already filled, and the vigor of auricular systole. Other things being equal, the earlier the auricular systole occurs, the more it contributes to ventricular filling. Various factors may affect the rate and time of filling. With increased venous return there is more rapid diastolic filling, but if the blood pressure is raised to the point of causing dilatation and decompensation, filling is delayed. With vagus slowing filling depends largely on the time at which auricular systole occurs. Studies of ventricular filling in man are difficult to make. Perhaps if we understood the factors on which the time of most rapid filling depended, we should be in a better position to understand the production of a gallop rhythm. There may be two times at which ventricular filling is most rapid, early in diastole, corresponding to the third heart sound, and at the time of auricular systole and the presystolic gallop.

It is not easy to correlate such theoretical considerations with clinical studies, but it has been noted that there may be a relation between the type of gallop and the heart rate. Pezzi[80] and Thayer[106] noted that an early diastolic sound is associated with rapid filling of the ventricles. Gubergritz[48, 49] made the same observation, and he also found that when the heart rate was increased the gallop sound

became less clear and occurred later, and that when the rate was slowed the sound became louder and more distinct. Müller[73] remarks on the frequent association of a presystolic gallop and a rapid heart in Graves' disease and also in animals when vagus control is removed.

We should like to know the result as well as the cause of the sudden rush of blood into the ventricles. The result is assumed to be sound produced by vibrations, but the question arises as to what structure vibrates. In an early paper Gallavardin[44] suggested that the interventricular septum might be deflected by the stream of blood entering the left ventricle until it hit against the wall of the right ventricle. It is hard to picture such a happening when blood is entering both ventricles at the same time. Einthoven[33] believed that the early diastolic sound was due to after-vibrations of the semilunar valves. This theory does not explain the shock, the fact that the sound is heard over the ventricles, or the mechanism of a presystolic sound. The two most popular theories are that the auriculoventricular valves are floated into a position of closure and caused to vibrate, and that the taut wall of the ventricle itself vibrates. The former theory is the more popular[101, 106] and has much to recommend it. The sound is heard in the region where mitral murmurs are most distinct; it is rather sharp for a muscle tone; pathologically, the sound occurs in cases where, because of a dilated ventricle or a sudden filling, conditions are suitable to produce vibrations of the valves.

On the other hand Wiggers[111] cites experimental evidence to show that the valves are not floated into position at this time and Bridgeman[19,20] points out that at the time of the third sound conditions are suitable for sound production due to muscle vibration. It is known that any sudden check in the movement of a tense muscle can result in sound production, and that it is not necessary for there to be sclerotic change in the heart muscle as was suggested by Potain. There is much to be said on both sides, but until we have more information, we are not in a position to say anything too definitely.

OCCURRENCE IN HEALTH AND IN DISEASE

In returning to the idea that the gallop is an exaggeration of a normal phenomenon, we inquire how often this phenomenon is found in health and under what conditions it is found in disease. Potain stated that a gallop was present in 20 per cent of normal persons, but it was usually considered rather a rare finding until Thayer observed a third heart sound in 65 per cent of healthy young persons. To bring out the sound Thayer suggested having the person exercise and then lie down either on his back or on his left side, or perhaps having the person lie down with his legs and arms held elevated by an assistant. These maneuvers tend to bring the apex nearer to the chest wall and to accelerate venous return. Obrastzow[75] found the third sound in 90

per cent of healthy individuals, Gubergritz[49] in 93 per cent, and Steinberg[104] in 95 out of 100 healthy children. All emphasize the fact that the third sound is overlooked unless sought particularly, and that it is brought out more clearly by the methods suggested by Thayer. Thus Steinberg found it in 78 cases while the child was standing but in 95 if the child lay down. As long ago as in 1855 Stokes[105] reported a case in which an early diastolic sound was present in the horizontal but not in the erect position. Why the sound is common in young persons and unusual at a later age we do not know. Thayer[106] suggests as important factors the thinness and elasticity of the chest wall and the absence of intervening lung. Whether these are the sole factors or whether there are differences in the state of the heart itself we do not know.

Clinically gallop rhythm is found in a number of different conditions. The classic presystolic gallop is associated with the beginning failure of the heart in cases of hypertension, chronic nephritis, or arteriosclerosis. The earliest descriptions note its relation to Bright's disease, and it is said to occur in about 80 per cent of the cases of "chronic interstitial nephritis."[8, 86, 79] Exchaquet[36] believed that it depended in some way upon the presence of albumin in the urine, this at a time when urine examinations were a new thing in hospital routine and when blood pressure readings were unknown. Potain at first associated gallop with albuminuria but later believed that its relation to increased arterial tension, a factor which he was unable to measure, was more common. The truth of this belief has been borne out beyond question. Increased tension, however, is not the only factor. As Müller[73] stated, if gallop depended on peripheral resistance, it should occur in cases of aortic stenosis. Kauffmann[63] was unable to correlate arterial tension and gallop, and it is generally agreed that gallop occurs only when the heart is beginning to show the effects of strain, to dilate, and to become insufficient to the demands put upon it. Kauffmann believed that the important factors were chronic dilatation or myocardial change. Gallop is also found with arteriosclerosis, aneurysm of the ventricle, coronary disease, adherent pericardium, emphysema or chronic displacement of the heart, as well as in acute conditions,—nephritis, gastrointestinal disorders, or acute infections, particularly diphtheria, scarlet fever, typhoid or acute rheumatic fever. Most French writers state that gallop does not occur with valvular disease, but we must remember that the third sound, considered by Thayer and others as equivalent to a protodiastolic gallop is the opening snap of the mitral or diastolic echo of the French, and is considered as distinct from gallop. This sound is particularly common in cases of mitral stenosis, aortic insufficiency, or adherent pericardium.[55, 58, 83, 106]

This bring us to the relation between the presystolic and protodiastolic gallops. According to one school the protodiastolic gallop is not merely an accentuation of the third sound, but is essentially a presystolic gallop in a rapidly beating heart.[88] According to another school the two are very different in the mechanism.[48] According to Thayer[106] the relation between the two needs more careful study.

Cuffer[27, 28] and his associates tried to explain the relation between the forms of gallop by assuming that with pure hypertrophy the gallop was protodiastolic, but that with hypertrophy and dilatation the gallop was presystolic. This opinion is not generally accepted, and Cuffer and Guinon[28] cite a case where a presystolic gallop was replaced by a protodiastolic one shortly before death. Potain,[86] Fraentzel,[41] Müller[73] and others have noted that a gallop might be presystolic at one time and protodiastolic at another. Laubry and Routier[66] reported a case in which the gallop was first presystolic, later mesodiastolic, and shortly before death was replaced by a rhythm with four sounds, — ∪ ∪ ∪. The most interesting report of differences in the time of the appearance of the third sound is that of Laubry and Mougeot.[65] They report a case in which a premature beat occurred after every third normal beat. With the first cardiac cycle following the premature beat the gallop was presystolic, with the second it was mesodiastolic, and with the third protodiastolic. Such reports as this seem to indicate that there are no very marked differences in the mechanism of the different types.

According to the theory that a protodiastolic gallop is merely a modification of the presystolic form, it is necessary to assume changes in the relative duration of different phases of the cardiac cycle. It has been shown that such changes may be present, but also that they are not necessarily present. Bordet, Yacoël, and Giroux[13, 47] studied the electrocardiographic changes and believed that the A-V conduction period was usually lengthened, the duration of systole increased, and the duration of diastole decreased. Gallavardin[43] found that in cases of gallop systole might make up 60 per cent of the total cardiac cycle. On the other hand Gubergritz[48] says that a split R-wave is the only constant sign of a presystolic gallop and that there is no constant sign of a protodiastolic gallop.

If we assume that a presystolic gallop is due to an audible auricular sound, we must admit that the two types of gallop are fundamentally different. If, however, we accept the theory that gallop is due to vibrations set up by a sudden rush of blood from auricle to ventricle, we can say that the two types are similar in cause. In any case we must agree that the relation between presystolic and protodiastolic gallop needs more study.

GALLOP RHYTHM AND CARDIAC ARRHYTHMIAS

The relation of gallop rhythm to cardiac irregularities is an interesting point. At first the reduplication of sounds caused by premature beats was confused with gallop, and Barié and Potain repeatedly warned against confusing gallop rhythm and intermittence of the pulse. They also noted that when there was irregularity the gallop sound was absent with the beats following the long silence. There are relatively few references to gallop in cases of cardiac irregularity. It is generally taught that when fibrillation appears, gallop disappears, but Lewis has shown that this is not necessarily true. Lewis[69] says that he has never found a presystolic gallop in a case of auricular fibrillation, but he has published graphic records of protodiastolic gallop sounds from cases of auricular fibrillation. He notes that the interval between the second and the gallop sound is too long for a simple reduplication and suggests that the sound is caused by vibrations of the auriculoventricular valves. If a presystolic gallop is due to the sudden rush of blood into the ventricle at the time of auricular systole, one would not expect to find this type of gallop in cases of fibrillation. In spite of the frequency of premature beats, the report of Laubry and Routier[66] is practically the only published description of a case of gallop associated with this type of irregularity. Vaquez[109] calls attention to gallop, extrasystoles, and tachycardia as a triad indicating failure of the left ventricle.

Pulsus alternans is the type of irregularity with which gallop is perhaps most commonly associated. Casual mention of this combination of signs is made by a number of writers, but the importance of the association is mentioned by few. Brauer,[18] Giroux,[47] Elliott,[34] and Laubry and Routier[66] have called attention to the fact that these two signs of a failing heart heart often go together; very few other writers mention the association at all. Certainly very few attach much importance to it. On the other hand Dr. Conner teaches that these are the two most common signs of a failing heart in a case of hypertension.

The importance of gallop rhythm as a sign of a failing heart has been pointed out ever since gallop was described, and this has been recognized, not only in papers and in textbooks, but also in clinical teaching. Gallop as a sign has been compared to angina as a symptom; gallop has been called the cry of the heart for help.[75] Case reports mention together gallop, pulsus alternans, nocturnal dyspnea, Cheyne-Stokes respirations, edema, cyanosis, precordial distress; and many of the case reports end with death. Certainly gallop is a serious symptom, and yet there are reports of patients in whom gallop was present off and on for years. Gallop is a sign which comes and goes; at first it may be present only on exertion, later even at rest. The disappearance of gallop is noted as a favorable sign, except in such

cases as the disappearance follows extreme cardiac dilatation and weakening of all the heart sounds. Several reports mention the change from a presystolic to a protodiastolic gallop before death. The seriousness of gallop as a sign applies particularly to cases of hypertension with broken compensation.[64] In young persons with acute infections the sign is not nearly so ominous. Indeed the gallop may then be a normal phenomenon. Gubergritz[49] points out that while a third sound is not in itself abnormal, it is always pathological for the third sound to be the loudest of the three. Pawinski[79] and Müller[73] believe that the prognosis is not so bad as is usually taught, that the gallop is a warning, an indication of fatigue, and Pawinski compares the presence of the third sound to the hitching of a third horse to a heavy wagon. The comparison suggests that gallop rhythm may have mechanical advantages, a suggestion that seems unwarranted. Laubry[65] calls gallop a sign of ventricular insufficiency, Lepine[67] a sign of fatigue, and Giroux[47] and Vaquez[109] an indication of decreased cardiac tone.

If gallop represents decreased cardiac tone and is a sign comparable to angina as a symptom, it is a sign which must not be overlooked and which should be better understood.

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Selected Abstracts

Sprague, Howard B.: Heart Attacks. Boston Med. and Surg. Jour., 1927, cxcvii, 472.

The expression of "heart attack" is used very loosely to explain a composite group of sudden or paroxysmal symptoms characterized by smptoms such as palpitation, dyspnea, chest pain, syncope, cyanosis or convulsions. In almost all instances of obscure subjective sensations about the thorax and head the heart is held responsible and it is blamed for all sorts of vasomotor effects from fainting to surgical shock. A large number of these are definitely related to heart abnormalities, but should be more accurately subdivided into such groups as have been suggested by the author.

Many such attacks are not cardiac in origin and the heart should not be held responsible for the symptoms. Certain conditions which are the real cause of such paroxysms have been noted.

Stress is laid on the importance in differential diagnosis of (1) a careful history of the exact symptomatology; (2) a consideration of the age and type of patient; (3) the physical findings apart from what can be found in the heart; (4) finally, the aid which can be secured from electrocardiographic and x-ray study.

Robinson, G. Canby: The Disturbances of Cardiac Function Leading to Heart Failure. South. Med. Jour., 1927, xx, 222.

In order to understand heart failure, the heart must be considered as part of the respiratory system, as its primary function is to furnish the motive power that carries oxygen from the lungs to every living cell of the body. In order to maintain a proper supply of oxygen to the cells of the body many physiologic functions must coordinate harmoniously and when this harmonious coordination is disturbed by the

failure of any one of these functions it may be very difficult or impossible for the body to reestablish it. The mechanism by which a cardiac lesion may disturb this cardiovascular respiratory system cannot be determined definitely on the basis of observed facts, but new facts are being collected which throw light on this subject and which bear on the treatment of heart failure.

In the first place there is satisfactory evidence to show that the output of the heart may be greatly increased when heart failure sets in. There is also evidence that reduction of the output of the heart is favorable to the establishment of its normal function through the relief of the symptoms of heart failure.

Another piece of evidence is that the effect of digitalis on the output of the heart is to reduce the average output by approximately 25 per cent.

The author states that in many cases of heart disease the evidence seems to point to the fact that the essential disturbance in the heart is a lack of perfect balance, between the two sides of the heart, especially between the right and left ventricles. He believes that an important effect produced by digitalis is the establishment of this perfect balance between the two sides of the heart, which is essential for properly regulating the circulation. This conception of heart failure is not a new or novel one. He emphasizes that the important new facts lend support to the correctness of the idea.

Griswold, Don M.: Heart Disease as a Public Health Problem. Am. Jour. Public Health, 1927, xvii, 101.

In this article the author presents tables and charts showing the occurrence of heart disease and the mortality rates of heart disease in the State of Iowa during the year 1925. These studies are statistical in nature.

He further emphasizes the relationship of heart disease to community health and vital statistics. He suggests several ways by which more accurate information may be obtained concerning the factors leading up to serious heart disease. He also discusses the newer aspects of heart disease as a community problem.

Clawson, B. J., Bell, E. T., and Hartzell, T. D.: Valvular Disease of the Heart with Special Reference to the Pathogenesis of Old Valvular Defects. Am. Jour. Path., 1926, ii, 193.

The primary object of this investigation was to trace the development of old valvular defects. This involved a detailed study of all forms of acute endocarditis, especially with reference to the manner of healing. The authors had available for study 280 cases of valvular heart disease, not including those of syphilitic origin.

In addition to the vegetations in acute endocarditis, there is a diffuse inflammation always in the free edge and often involving the greater part of the leaflet. This circumstance explains the uniform thickening so commonly seen in old defective valves.

Rheumatic vegetations are composed chiefly of fibroblasts, and in the process of healing they readily become converted into fibrous tissue. There is no ulceration and no organization. Fifty-five of seventy-three old defective valves were considered the result of rheumatic endocarditis, and in twenty-seven of these, incompletely healed lesions were recognizable.

Bacterial endocarditis is a more intense inflammation than the rheumatic. Proliferation predominates but exudation is often prominent. Large thrombi are formed on the raw surfaces and there is often ulceration. Healing consists in the conversion of the leaflet into scar tissue. Such portions of the thrombi as do not become detached, persist indefinitely without becoming organized, although they may become calcified. Complete healing rarely occurs. Three of seventy-three old defective valves were interpreted as the result of bacterial endocarditis.

Transitions between rheumatic and bacterial vegetations are frequently seen. Rheumatic vegetations were found in association with bacterial in three-fourths of the cases of subacute bacterial endocarditis.

Fifteen of seventy-three old defective valves belonged to the aortic calcified nodular group. The etiology of this type is unknown. There is no satisfactory evidence that it is of inflammatory origin, and it seems unrelated to atheroma. Aortic stenosis in the absence of disease of any other valve is usually of this form.

Stenosis is more frequent than insufficiency in old defective valves.

The only old pulmonary valve defects seen were of the congenital type (three cases of pulmonary stenosis).

An acute rheumatic endocarditis may terminate in several different ways: (a) death during the acute stage from toxemia; (b) partial or complete healing followed after a variable interval by the reappearance of fresh rheumatic vegetations (recurrent rheumatic endocarditis); (c) partial or complete healing followed by the formation of bacterial vegetations on the valves—a more active inflammation (subacute bacterial endocarditis); (d) slow incomplete healing giving rise to deformed leaflets on which rheumatic inflammation is still recognizable; (e) complete healing resulting in thickened, stiffened valves with smooth surfaces.

As to pathogenesis, 76 hearts with old valvular defects are interpreted as follows: 55 from rheumatic endocarditis, 3 from bacterial endocarditis, 15 (all aortic stenosis of the calcified nodular type) of undetermined origin, and 3 (pulmonary stenosis) congenital.

McPhedran, F. Maurice, and Weyl, Charles N.: Clinical and Physiologic Deductions from Synchronized Roentgen-Ray Exposures. Am. Jour. Med. Sc., 1927, clxxiii, 313.

A description of the method of synchronizing roentgen ray exposures with selected phases of the cardiac cycle, and a brief preliminary report of some deductions from such exposures has already been given by the authors. Since that report the Weyl pulse relay has been routinely employed in studies of the chest of both adults and children in the Henry Phipps Institute.

They conclude that there is evidence that cardiac movement and vascular pulsation cause more extensive and complex pulmonary movement than has hitherto been recognized. The effects of vascular displacement and vibration in the blurring of roentgenographic detail are important. Artefacts are produced to which have been given a pathologic interpretation. By synchronization of exposures with late diastole such artefacts may be eliminated and finer detail both normal and abnormal recorded with marked enhancement of stereoscopic accuracy. The method is of value in the early recognition of the differential diagnosis of discreet tuberculous infiltrations, especially those which are infantile in type, beginning bronchiectasis, bronchopneumonia and other processes manifesting themselves by changes in the relative density of the pulmonary structures with slight and equivocal or no physical signs.

Saphir, Otto: Rupture of the Heart by Indirect Trauma in a Four-Year-Old Boy. Am. Jour. Med. Sc., 1927, clxxiii, 353.

The author reports a case of rupture of the heart in a boy, aged four years. He was the victim of an automobile accident, in which he was struck apparently in the region of the right hip, with fractures of the right pelvic and iliac bones. There was no evidence of injury to the chest. No pathological changes other than the rupture in the heart were demonstrable. The lymphoid apparatus in general was hyperplastic. The author feels that spontaneous rupture could not be definitely excluded. While blows to the chest could not be excluded, they saw no evidence of injury to

the chest wall. The myocardium showed no evidence of previous disease; therefore, the most probable explanation is that the rupture of the heart is dependent on the trauma in which the greatest force was exerted in the region of the right pelvis.

Kahn, Morris H.: Tender Spots on the Chest Wall in Angina Pectoris. Am. Jour. Med. Sc., 1927, clxxiii, 363.

Hyperesthesia of areas on the chest wall is commonly found in association with anginal pain. It is referable to the impaired nutrition of the heart wall and to the sensitiveness of the aorta and coronary artery area. It is often complained of by the patient and can be definitely localized objectively.

Of 55 patients with angina pectoris, 48 presented tender spots along the ribs or on pressure over the sternum. This sign was found positive in nonanginal cases with aortic or myocardial disease. In individuals without heart involvement, tender spots on the chest wall were not found in any case.

In cases of angina pectoris, the tender spots are most often located on the second, third, and fourth ribs to the left of the sternum (fourth cervical and second and third thoracic) and over the second and third ribs in the outer part of the right pectoral region (fourth cervical).

The tender spots on the chest wall persist for a long time after an attack of angina pectoris and sometimes continue throughout the intervals between attacks.

They are especially valuable in the differential diagnosis between myocardial lesions and affections of the upper abdominal viscera.

Waite, Willis W.: The Nature and Distribution of the Lesions in Syphilitic Aortitis. Am. Jour. Med. Sc., 1927, clxxiii, 357.

In a continuous series of 300 postmortems, the author observed 33 cases of syphilitic aortitis. From a study of these cases it can be stated that syphilis may attack the aorta either locally or generally, more usually the latter. One portion may suffer severely and the rest only slightly. The first or ascending portion usually suffers more and the rest less severely, but the whole process is similar and is a strangulation necrosis caused by periarteritis and obliterating endarteritis of the vasa vasorum which starves and destroys the elastic layer. When the condition is violent, it travels as a serpiginous ulcer, causes aneurysms and a vegetative growth on the intima which may break off and form emboli. The most usual site for serpiginous ulcers is in the first portion, apparently due to the anatomical structure, but the ulcers, wherever found, are due to a sudden cutting off of the blood supply to the area involved.

Marvin, H. M.: Digitalis and Diuretics in Heart Failure with Regular Rhythm with Especial Reference to the Importance of Etiological Classification of Heart Disease. Jour. Clin. Investigation, 1927, iii, 521.

It is the purpose of this paper to call attention to the importance of etiological classification of heart disease in estimating the results of digitalis therapy and to add certain observations concerning the action of digitalis or diuretic drugs upon the signs and symptoms of heart failure in the presence of a regular rhythm. It should be emphasized that many observations which have been interpreted as indicating excellent results from the administration of digitalis to patients without normal cardiac rhythm are entirely unacceptable because the observers failed to take into account the influence of bodily rest. It is clear, however, that this preliminary rest period is essential to the proper interpretation of results only when benefit follows the administration of the drug. In this study adults with advanced congestive heart failure and considerable edema with regular cardiac rhythm and without evidence of nephritis were selected and placed at complete rest with no medication other than necessary sedatives. The fluid intake was restricted usually to 1200 c.c. per day, the

twenty-four-hour volume of urine measured, and the body weight determined every day or every other day. The period of rest was terminated when it appeared that maximal improvement had been secured or when the condition of the patient had grown so much worse as no longer to justify withholding of useful medication. In the cases under consideration it varied from four to twenty-two days. At the conclusion of this preliminary period digitalis was given in large amounts within a short time. Two or three days were allowed to elapse after the administration of the full dose of digitalis. It was then started in maintenance doses. If satisfactory diuresis and complete disappearance of the edema occurred as the result of digitalis therapy, no other drug was used. If, on the contrary, there was little or no benefit from digitalis, it was followed, after an interval of about a week, by one or more diuretics of the xanthine group.

The author divides the cases selected into three main groups: those with rheumatic heart disease, those with syphilitic heart disease, and those with arteriosclerotic heart disease. The administration of digitalis in suitable doses under properly controlled conditions to patients with advanced heart failure, regular rhythm, and considerable edema appears to cause improvement consistently in only the arteriosclerotic heart disease group. The drug has been found occasionally beneficial in patients with syphilitic heart disease, but almost devoid of effect in rheumatic heart disease. The same differences have been noted with regard to the effectiveness of diuretic drugs administered after complete digitalization. Individuals with rheumatic heart disease seldom show satisfactory diuresis. Those with arteriosclerotic heart disease, as a rule, respond in a highly favorable manner.

The foregoing statements are supported by the results in 20 illustrative cases analyzed in the accompanying table, but are actually based upon the study of more than twice that number.

It is suggested that differences of opinion concerning the effect of digitalis in heart failure with normal rhythm may depend in part upon differences in the patients selected for treatment. It is believed that a division of patients upon the basis of etiology of the heart disease is essential for the proper correlation of the different observers.

Howard, Tasker: Double Tachycardia. Am. Jour. Med. Sc., 1927, clxxiii, 165.

The author reports a case of double tachycardia occurring as a result of digitalis medication. The electrocardiograms showed an A-V dissociation with independent auricular and ventricular tachycardia. The ventricular rate was 160 and showed a normal supraventricular form to the ventricular complex, the ventricular tachycardia evidently originating in a focus lying between the A-V node and the bifurcation of the bundle. The patient had received digitalis because of orthopnea and weakness during the latter part of the pregnancy.

Lawrence, John S., Hurxthal, Lewis M., and Bock, A. V.: Variations in Blood Flow with Changes in Position in Normal and Pathological Subjects. Jour. Clin. Investigation, 1927, iii, 613.

The work reported in this paper was undertaken with the following objectives in view: (a) correlation of the various factors entering into the physiology of circulation under varying conditions and (b) comparison of the circulatory responses of certain pathologic individuals with those obtained in normal subjects.

The work includes simultaneous measurements of blood flow, rate of ventilation, metabolic rate, pulse rate, pulse pressure, cardiac output per systole, vital capacity, tension of CO_2 in alveolar air and tension of CO_2 in arterial and mixed venous blood with changes of position.

In normal subjects the blood flow, pulse pressure, and tension of carbon dioxide in alveolar and mixed venous air samples diminishes as one changes from the lying to the sitting or standing postures. In normal subjects the ventilation, metabolic rate, pulse rate, vital capacity and difference in tension between CO_2 in alveolar air and mixed venous air samples increase from the lying to sitting or standing position.

The subjects showing pathological conditions have been too few in number to admit of definite reliable conclusions, but at least they do indicate that responses different from the normal may be obtained in some instances. The authors have studied patients with exophthalmic goiter, a small group of patients with myxedema, patients with rheumatic heart disease and a group of convalescent postoperative patients in the hospital.

Von Glahn, William C., Pappenheimer, Alwin M.: Specific Lesions of Peripheral Blood Vessels in Rheumatism. Am. Jour. Path., 1926, ii, 235.

The authors describe a peculiar type of vascular inflammation which they have found in a series of cases of rheumatic carditis which they believe to be specific and characteristic. In this paper they describe the distinctive features of these lesions and present detailed evidence in favor of their rheumatic origin. The material studied consists of a series of 47 consecutive cases of rheumatic heart disease and the lesions which were found in 10 of these cases.

These lesions are characterized by the exudation of fibrin into and about the vessels, by distinctive changes in the cellular reaction in the adjacent tissues, and by the absence of thrombosis. These acute lesions are followed by organization with or without formation of new collateral channels within the thickened intima and occasionally within the muscular layer.

Goldstein, Bertram, and Boas, Ernst P.: Functional Diastolic Murmurs and Cardiac Enlargement in Severe Anemias. Arch. Int. Med., 1927, xxxix, 226.

Cardiac dilatation, often accompanied by cardiac hypertrophy, is a common finding in patients with severe anemias. Diastolic murmurs resembling those of aortic insufficiency are heard in about 10 per cent of patients with pernicious anemia. These are caused not by organic valvular disease but by a relative insufficiency of the aortic valve. In a smaller number of anemic patients, presystolic murmurs may be present in the absence of mitral stenosis. In patients with severe anemia the presence of cardiac enlargement, a mitral configuration of the heart, and a diastolic or presystolic murmur does not warrant the diagnosis of organic valvular disease.

Oppenheimer, B. S., and Stewart, Harold J.: Dependence of the Form of the Electrocardiogram upon the Site of Mechanical Stimulation of the Human Ventricles. Jour. Clin. Investigation, 1927, iii, 593.

The authors were given an opportunity to investigate the relation of the form of the electrocardiogram to the site of stimulation in the ventricles in a patient whose ribs on the left side had been removed in the course of a modified Estlander operation for empyema some 25 years before. Over the left lateral chest wall the contractions of the auricles and ventricles were distinctly seen and felt through the soft tissues. By appropriate mechanical stimulation they were able to elicit premature contractions from either ventricle or auricle. They report in this paper the results obtained by such artificial stimulation, more particularly of the ventricles.

The premature contractions fall into three groups on the basis of their form: those having upward deflections in Lead III, those having downward deflections in Lead III and those having diphasic deflections in Lead III. Although it was not possible to identify which portions of the ventricles lay beneath all points stimu-

lated, it is reasonably certain that when a point definitely over the right ventricle was stimulated, the spiked deflections in the electrocardiogram and the premature contractions were upright in Lead III and inverted when the point stimulated was over a left ventricle. To retain the terminology which is in current use seems therefore justifiable.

Stewart, Harold J., and Crawford, J. Hamilton: The Effect of Regular and Irregular Tachycardias on the Size of the Heart. Jour. Clin. Investigation, 1927, iii, 483.

This study is concerned with the effect of tachycardia on the size of the heart in normal unanesthetized dogs. In four dogs the authors observed the effect of regular tachycardia on the size of the heart. This size was decreased during the period of tachycardia in all of the observations. The decrease varied between 7 and 14 per cent. Artificial tachycardia was maintained at about 300 beats per minute.

In three dogs they were able to compare the effect of regular and irregular tachycardia on the size of the heart. During auricular fibrillation the size of the heart was unchanged in two observations and was increased 11 per cent in the third.

Andrus, E. Cowles, and Carter, Edward P.: The Mechanism of the Action of Hydrogen Ion upon the Cardiac Rhythm. Jour. Clin. Investigation, 1927, iii, 555.

The authors have for some time been engaged in studying the effects of hydrogen-ion concentration upon the normal rhythm of the isolated heart. The results of these studies previously reported have shown that it is possible to control the rate of sinus or nodal rhythm by changes in the P_H of the Locke perfusate between the limits of P_H 7.0 and P_H 7.8. With a rise of C_H the propagation of the excitatory process as represented by the P-R interval is retarded. When a perfusate is replaced by one slightly more alkaline, A-V transmission is accelerated. Intraauricular conduction is similarly affected. The inhibitory action of the vagus is enhanced at P_H 7.0 and decreased by P_H 7.8 to 8.0. Sympathomimetic substances, on the other hand, are far more effective at P_H 7.8 than at P_H 7.0. And finally, the refractory period of both auricular and ventricular muscle has been shown to vary with the reaction of the perfusate, being lengthened at P_H 7.0 and shortened at P_H 7.8.

It has been suggested that changes in C_H may produce their effects indirectly by affecting the ionization of the calcium. The amount of active calcium ion in such a mixture as Locke's solution is dependent chiefly upon the P_H and the concentration of bicarbonate, decreasing as these factors increase. The authors have, therefore, undertaken to study the effects of various concentrations of calcium in Locke's solution with the same P_H.

In all the experiments, dog's hearts were perfused through the coronary arteries by methods previously described and galvanometric records taken by direct leads.

From their study it seems unlikely that the effects of alteration in P_H are to be explained by the resultant changes in the ionization of calcium. Such possible effects as have been reported seem directly opposed to such a conclusion. Since an increase in calcium has, if any, an augmentatory action, whereas increase in P_H is per se consistently depressant.

In the course of a series of experiments upon the isolated rabbit's auricles it was found that equal changes in P_H produced quantitatively different effects upon the rhythm, depending upon the acid employed. These results led the authors to investigate the effects upon the rhythm of different concentrations of carbonic acid at the same P_H. An increase in the carbonic acid content of the perfusate accentuates the spontaneous development and propagation of the excitatory process.

The authors conclude, therefore, that the cardiac tissue is peculiarly sensitive to

alterations in hydrogen-ion concentration, whether this occurs in the cell itself, through products of its own metabolism, or by alteration in the P_H or CO_2 content of the fluid bathing it, and suggest that the difference in hydrogen-ion concentration within and without the cell is a factor controlling its excitation.

Wiggers, Carl J.: Studies on the Cardiodynamic Actions of Drugs. I. The Application of Optical Methods of Pressure Registration in the Study of Cardiac Stimulants and Depressants. Jour. Pharmacol. and Exper. Therap., 1927, xxx, 217.

With the introduction of optical methods of pressure registration, the dynamic factors controlling the vigor of the heartbeat under normal and pathological conditions have become reasonably well understood. In this communication, an attempt is made to analyze the principles and methods through which the facts thus gathered may also be applied to the study of cardiac stimulants and depressants.

The heartbeat can be altered by influences classified as primary and secondary, i.e., by those that affect the heart muscle or cardiac nerves directly and by those that indirectly affect it through changes in arterial resistance or initial tension and length. The established effects of these secondary influences on the heart are reviewed and summarized, and previously unrecognized factors in determining initial tension and length are discussed.

In order to separate the primary stimulating or depressing action of a drug from the secondary effects of its peripheral action, it is necessary to record intraventricular and aortic pressure curves optically when the heart is working under constant dynamic conditions. The heart rate is kept constant by rhythmic artificial stimulation of the right auricle, at a rate somewhat in excess of the natural. The arterial resistance is kept the same by applying a special clamp to the aorta and by increasing or decreasing the constriction thus produced when a drug causes peripheral changes which alter the arterial resistance. Emphasis is laid on the fact that the arterial resistance represents the diastolic load against which blood must be expelled, and that constancy in the diastolic pressure is the only criterion of an unaltered arterial resistance.

Reasons are given why the initial tension cannot be accurately controlled either in the intact animal or in the heart-lung preparation. The effects due to such changes in initial tension can usually be separated from those produced by the action of a drug, for only two variables enter into this reaction, and the effects of one are known.

Primary cardiac action of a drug may mean (a) that similar effects are produced in all units of cardiac tissue, (b) that the number of fractions partaking in contraction has altered, or (c) that changes in the summation of entering fractionate contractions have occurred. These may be differentiated by determining the differences in excitation times on the ventricular surface (interpunctual intervals) before and during the action of drugs.

Wiggers, Carl J.: Studies on the Cardiodynamic Actions of Drugs. II. The Mechanism of Cardiac Stimulation by Epinephrin. Jour. Pharmacol. and Exper. Therap., 1927, xxx, 233.

By registering the intraventricular and aortic pressures by optically recording manometers, while the heart rate is kept constant and the arterial resistance is controlled through a special aortic clamp, it is possible to separate the primary and secondary factors concerned in the stimulating action of epinephrin on the mammalian ventricles.

By recording, in addition, the relative moments that intrinsic negativity develops over various points of the ventricular surfaces, it is possible to calculate the "inter-

punctal differences'' in the onset of negativity, and so analyze the part that changes in ventricular conduction play in the stimulating effect of this drug.

The evidence presented indicates that epinephrin is capable of producing an increased gradient of the isometric pressure rise, a higher pressure maximum, an abbreviated systole, a steeper isometric relaxation gradient, an earlier termination of relaxation, and a more complete diastolic relaxation by affecting the vigor and velocity of individual fractionate contractions, directly. In some instances, but by no means in all, an increase in the velocity of excitation and a more rapid summation of the individual fractionate contractions, further increase the velocity of the pressure development and the height of the pressure maximum and tend to abbreviate systole still more. The greater diastolic relaxation, or increased initial length may aid in producing the steeper gradient of isometric contraction and the higher pressure maximum but tends to lengthen the duration of systole. Since initial tension decreases at the same time, such alterations in initial length cannot be attributed to passive or secondary influences; but must be referred to a primary action of the drug on the heart. This is substantiated by the observation that the isometric relaxation gradient is steeper and the curve falls to a lower level at the beginning of diastolic filling.

In addition, there are secondary effects of the drug which help to intensify the stimulating action of epinephrin. Most important is the increased arterial resistance produced by the peripheral vascular action of the drug. This causes a later opening of the semilunar valves, a slight prolongation of isometric contraction, a higher pressure maximum, and a further abbreviation of systole.

Wiggers, Carl J., and Stimson, Barbara: Studies on the Cardiodynamic Actions of Drugs. III. The Mechanism of Cardiac Stimulation by Digitalis and g-Strophanthin. Jour. Pharmacol. and Exper. Therap., 1927, xxx, 251.

The mechanism of ventricular stimulation by digitalis and g-strophanthin was studied by methods described in preceding papers of this series.

Records and data are presented and analyzed. They lead to the conclusion that digitalis substances exert a direct stimulating effect on ventricular muscle which manifests itself by an increased gradient of pressure development, a higher pressure maximum within the ventricle, a reduction in the period of systolic contraction and, under certain conditions, by a more rapid isometric relaxation. Digitalis substances produce such effects by increasing the velocity of fractionate contractions, by shortening their duration, and by increasing the speed of their relaxations. Increased rate of fractionate summation does not occur, in fact the stimulating influence persists in some cases where the entry of fractionate contraction is retarded as a result of delayed ventricular excitation.

This primary action has, however, been overestimated and is demonstrated neither by the larger systolic discharge nor by characteristic effects on the ventricular pressure curve alone.

This primary action of digitalis is supplemented, and in some cases preceded, by the secondary influence of an increase in initial length. This is naturally accompanied by an increase in initial tension, but the latter may be reduced by greater speed of isometric relaxation so that initial tension remains unchanged or becomes even less than normal. In either event, such an increase in initial length can account for all the changes in the intraventricular pressure curve, except the tendency of systole to shorten, and of isometric relaxation to occur more rapidly.

When the diastolic arterial pressure is not controlled and rises as a result of the drug's action, the increased arterial resistance so occasioned, influences the vigor of the ventricular beat to a very considerable degree. It contributes to the elevation of initial tension and causes a further increase in diastolic length by ''back pressure

effects.'' In consequence, it favors a steeper gradient, a higher pressure maximum, and a larger systolic discharge. The latter occurs in spite of a further reduction in the phase of ejection and as a result of the increased velocity of ejection.

At no stage of digitalis action is systolic discharge reduced or the diastolic size of the ventricles decreased as long as the rate of the heart is kept constant. Such effects are produced only by cardiac acceleration.

Sidel, Nathan, and Dorwart, Frederick G.: Quinidine Sulphate in Auricular Fibrillation. Bost. Med. and Surg. Jour., 1927, cxcvi, 216.

This report on the treatment of auricular fibrillation with quinidine is presented primarily to demonstrate the desirability of giving larger doses of the drug than are usually administered. The series consists of 20 unselected cases of auricular fibrillation admitted to the medical service of the Boston City Hospital. It includes one patient with ventricular fibrillation and a boy ten years old showing auricular fibrillation. Practically all of the patients were admitted because of varying degrees of heart failure as described in the case reports. The ages range from 10 to 83. All were chronic established fibrillators. Rheumatic heart disease in 7 and arteriosclerotic myocarditis in 13 were the underlying conditions. The dosage was increased gradually, if regular rhythm did not result. It is significant that of the 13 cases that reverted to normal rhythm 7 required a daily dosage of 75 grains and more before regularity occurred. Regular rhythm under quinidine therapy resulted in 100 of the patients with a cardiac history of two years or less. All of the cases except one had recent heart failure. All except one became compensated with digitalis, etc., before quinidine was started.

The highest single dosage was 45 grains. The highest daily dosage was 200 grains. The highest total dosage producing regular rhythm was 920 grains. The highest total dosage over a period of two months was 3381 grains.

It is emphasized very strongly that large doses of quinidine are not being advocated. This report simply shows that large divided doses of quinidine can be given after small doses have been tried and found unsuccessful. If larger amounts are to be given in the gradually increased dosage used in this series, the patient should be hospitalized so that his condition may be followed carefully.

McFarlane, A., and Masson, G. A.: On the Standardization of Digitalis by the Cat Unit Method. Jour. Pharmacol. and Exper. Therap., 1927, xxx, 293.

The authors have attempted to determine the reason for the varying results in the Hatcher-Brody method of assay of digitalis which occur in Edinburgh as compared with other places.

As the result of this study they feel that there are probably two groups of cats being dealt with. The relatively high results belong to a small and apparently distinct group of animals with a greater resistance to the drug. The presence of this small group of cats may cause pronounced variations in the estimation of the strength of digitalis powder, as only a small number of animals have been used for each assay.